Archives of Neurology and Psychiatry

VOLUME 26 DECEMBER, 1931 NUMBER 6

FIRST INTERNATIONAL NEUROLOGICAL CONGRESS

PRESIDENTIAL ADDRESS *

B. SACHS, M.D.
NEW YORK

On behalf of the members and friends of this First International Neurological Congress, I wish to thank Mr. Motta, vice president of the Swiss Federation, the City and Canton of Berne, the university authorities, the medical societies, the Swiss committee and the people of Berne for the cordial reception given us and for their sympathetic greetings.

We neurologists are happy to meet in the very heart of this glorious Swiss country, to enjoy its soul-stirring scenery, its marvelous lakes and mountains, its fine cities; to learn to know its sturdy people, and to be inspired by the memories of those early days, over six centuries ago, when Swiss heroes made the first successful stand for human liberty.

It must be a great satisfaction to the government and to the people to realize that they are extending their hospitality in this period of world stress to a fraternity of medical men in forty-three different countries, who, irrespective of national boundaries, and often at a great personal sacrifice, have come from every corner of the globe to further the special science to which they are devoted and incidentally to promote international friendship and the well-being of their fellowmen in every land.

To all the members of this congress and to their friends here assembled, I bid a hearty welcome. It was the proud privilege of the American Neurological Association to undertake the formation of this congress, but we could not have succeeded without the enthusiastic support of the delegates from every country and above all without the skilful cooperation of the Swiss committee and its most efficient secretaries.

That you elected me president of this First International Neurological Congress is an honor, which I appreciate deeply, and a distinction that I scarcely deserved. I have tried to merit your approval by working earnestly with the other members of the program committee for the success of this meeting. We have endeavored to be absolutely impartial, and to do justice to all, so far as that was humanly possible. If we have

* Submitted for publication, Oct. 27, 1931.

* Read before the First International Neurological Congress, Berne, Switzerland, Aug. 31, 1931.

erred, be generous and consider the difficulties to be overcome. Whatever my own personal shortcomings may have been, I have one confession to make: My heart has been in this task, and the task was worth the doing.

The purpose of this congress is primarily to establish personal contact and to unite neurologists of the entire world in the attempt to find a solution to the many important problems engaging their attention; to indicate other problems that will call for study in the immediate future, and to emphasize the important relation that neurology bears to every branch of medical and surgical science. Neurology is the fundamental specialty of medical art. Without a thorough appreciation of its truths, medical and surgical science is like a ship floundering about in a turbulent sea without helm or rudder.

In the last decades of the nineteenth and in the first of this century, neurology contributed mightily to the startling advances in general medicine and surgery; it shared honors with bacteriology; it gave birth to modern psychiatry through its revelation of the structure and function of the brain; and the end is not yet. To realize the full extent of this influence, and at the same time to do homage to our predecessors and teachers, let us recall the work of Charcot, greatest of clinical masters, of Joffroy, of Raymond, of Dejerine, of dear Pierre Marie; the ingenious doctrines and the deep philosophy of Hughlings Jackson—the centenary of whose birth is soon to be celebrated—recall the work of Ferrier, of Gowers, of Byrom Bramwell, whose recent death we deplore, of Horsley, the great promoter of neurosurgery; recall the splendid achievements of Tuerck and Romberg, or Erb and Westphal and Struempell, of Fritsch and Hitzig, of Oppenheim, of Meynert and Wernicke and Edinger, of Obersteiner, of von Monakow and Forel, of Golgi and Mingazzini, of Ramón y Cajal, of Weir Mitchell, of Seguin, of Spitzka, of Dercum and Mills, whose death only a few months ago has meant a great loss to neurology in America.

Were I permitted to mention the work of those still active, many of whom are fortunately with us today, it would help us to realize what medicine and the specialties owe to neurology. Neurologic data are of vast importance in ophthalmology, in otology, in laryngology, in pediatrics, in cardiac and gastro-intestinal disorders, and surely in diseases of the kidneys, as Charcot described so brilliantly. Consider the important relations to the ductless glands, and to all problems of heredity. A thorough knowledge of neurology should play an important part in every medical curriculum, and in every hospital nervous disorders should be treated in special wards and by men especially trained and fitted for such work. We neurologists have suffered from an excess of modesty, or a

minimum of assertiveness, while others have cried from the housetops. The proceedings of this congress will, I am certain, give ample evidence of the importance of neurology in the medical and surgical sciences. But let me add that we recognize a definite reciprocal relation with medicine, with surgery and with psychiatry. Mental and nervous diseases cannot be studied apart. In neuroses and psychoneuroses, established neurologic data furnish the reliable background and the criteria by which all new theories, however fanciful, are to stand or fall. With neurosurgery we are so intimately and permanently allied that divorce is unthinkable. The neurosurgeon must be steeped in neurology, and the neurologist must follow with keenest interest the work done by the neurosurgeon. Our program proves that the neurosurgeons and the pure neurologists, if any of us are pure, have identical problems.

CUTANEOUS SENSORY FIBERS AND SENSORY CONDUCTION *

S. W. RANSON, M.D.
CHICAGO

When mechanical, thermal or chemical stimuli of sufficient intensity are applied to the skin, they evoke sensations of pain. At one time it was thought that excessive stimulation of any cutaneous receptor was painful, but this view was abandoned when Donaldson, von Frey and others found that there were definite touch, temperature and pain spots on the skin. According to Adrian,[1] "It is now believed that there are special receptors and conductors for pain as there are for touch and temperature, but the specific character of pain, its urgency, massiveness, etc., suggests that the receptors and conductors differ considerably from those of other types of cutaneous sensation."

It has been said that there are not enough sensory fibers to supply the entire surface of the body with specific conductors for each of the varieties of cutaneous sensation. Ingbert[2] made careful counts of the myelinated fibers in the dorsal roots of man, and on the basis of the information thus obtained, he estimated that one cutaneous nerve fiber innervates, on the average, 1.08 sq. mm. of the skin of the head and neck, 1.3 sq. mm. of the skin of the arm, 2.45 sq. mm. of the skin of the leg and 3.15 sq. mm. of the skin of the trunk. He stated that if there are four classes of cutaneous nerve fibers, each fiber would have to supply an area four times as large, which in the case of the dermal surface of the trunk would amount to 12.6 sq. mm. Ingbert counted only myelinated nerve fibers; at the time he was working, it was not known that there are many sensory fibers that do not possess myelin sheaths. The discovery of unmyelinated sensory fibers in large numbers more than doubles the known sensory supply for the skin and largely invalidates the argument that there are so few fibers that each must convey several varieties of sensation. My purpose in the present

* Submitted for publication, March 30, 1931.

* From the Institute of Neurology, Northwestern University Medical School.

* Read before the Section on Neurology and Psychiatry of the New York Academy of Medicine and the New York Neurological Society, Jan. 13, 1931.

1. Adrian, E. D.: The Basis of Sensation, New York, W. W. Norton & Company, 1928.

2. Ingbert, C. E.: An Enumeration of the Medullated Nerve Fibers in the Dorsal Roots of the Spinal Nerves of Man, J. Comp. Neurol. **13**:53, 1903; On the Density of the Cutaneous Innervation in Man, ibid., **13**:209, 1903.

paper is to review the evidence concerning these unmyelinated fibers and to discuss their probable function.

It has long been known that there are many more cells in the spinal ganglia than there are myelinated sensory fibers in the dorsal roots and spinal nerves. This statement is based on accurate counts. Gaule and Lewin [3] found 20,361 cells in the first coccygeal ganglion of the rabbit and 3,173 myelinated fibers in the corresponding dorsal root. In the white rat, Hatai [4] found 12,200 cells in the sixth cervical ganglion, 4,227 fibers in the corresponding dorsal root and 9,442 cells for 1,644 fibers in the second lumbar nerve. My own counts on the second cervical nerve of the white rat showed that there were 7,721 cells in the spinal ganglion for 2,472 myelinated fibers in the dorsal root; [5] that is to say, there are from three to six times as many cells as myelinated sensory fibers.

Since the number of myelinated fibers in the mixed nerve distal to the ganglion is only slightly greater than the sum of these fibers in the ventral and dorsal roots, the number of myelinated sensory fibers in the nerve is approximately the same as that in the dorsal root.[5] How can one account for this excess of spinal ganglion cells over myelinated sensory fibers? It might be assumed that many of the cells had no axons if it were not for the fact that after section of the nerve at least 85 per cent of all of the cells in the ganglion show a typical axonal reaction (Köster,[6] Lugaro,[7] Warrington and Griffith [8] and Ranson [9]).

The excess of spinal ganglion cells over myelinated dorsal root fibers and the occurrence of chromatolysis in the vast majority of these cells after section of the nerve led me to look for unmyelinated fibers arising in the ganglion.

Examination of the spinal ganglia of the dog, stained by the pyridine-silver method,[10] showed that the small cells of these ganglia give

3. Gaule, J., and Lewin, T.: Ueber die Zahlen der Nervenfasern und Ganglienzellen in den Spinalganglien des Kaninchens, Centralbl. f. Physiol. **10**:465, 1896.

4. Hatai, S.: Number and Size of the Spinal Ganglion Cells and Dorsal Root Fibers in the White Rat at Different Ages, J. Comp. Neurol. **12**:107, 1902.

5. Ranson, S. W.: The Architectural Relations of the Afferent Elements Entering into the Formation of the Spinal Nerves, J. Comp. Neurol. **18**:101, 1908.

6. Köster, G.: Ueber die verschiedene biologische Werthigkeit der hinteren Wurzel und des sensiblen peripheren Nerven, Neurol. Centralbl. **22**:1093, 1903.

7. Lugaro, E.: On the Pathology of the Cells of the Sensory Ganglia, Rev. Neurol. & Psychiat. **2**:228, 1904.

8. Warrington, W. B., and Griffith, F.: On the Cells of the Spinal Ganglion and on the Relationship of Their Histological Structure to the Axonal Distribution, Brain **27**:297, 1904.

9. Ranson, S. W.: Alterations in the Spinal Ganglion Cells Following Neurotomy, J. Comp. Neurol. **19**:125, 1909.

10. Ranson, S. W.: The Structure of the Spinal Ganglia and of the Spinal Nerves, J. Comp. Neurol. **22**:159, 1912.

rise to unmyelinated fibers which divide, just as do the myelinated fibers coming from the large cells, into a branch that is directed peripherad into the nerve and a finer branch that is directed centrad into the dorsal root (fig. 1*E*). There was nothing new about this observation. It coincided fully with the earlier observations of Dogiel [11] and Cajal.[12] What was new was the recognition of the fact that these small cells and their unmyelinated axons are very numerous, more numerous in fact than the large cells and myelinated fibers.

The myelinated axons stain a light yellow in pyridine-silver preparations and are surrounded by unstained space representing the myelin sheath. The unmyelinated fibers stain selectively and are dark brown or black. They contrast sharply with the light yellow and much coarser myelinated fibers. As is shown in figure 1*E*, the bifurcation of the unmyelinated axons into central and peripheral branches occurs at a slight triangular expansion in the fiber and without any change in the intensity of the stain. In the myelinated fibers the bifurcation occurs at a node of Ranvier, and the axon appears constricted and stains more deeply at the place where it divides. This difference in the appearance of the bifurcations is characteristic for the two types of fibers. It is important to note the difference in size of the two branches. The central branch is very small and often appears to be not more than one-third the diameter of the peripheral branch. These fine fibers are directed centrad in the dorsal roots to the spinal cord.

In a longitudinal section, taken at the point where the roots fuse to form the nerve, the peripheral branches of the unmyelinated fibers can be followed from the ganglion into the mixed nerve, to be distributed in both the ventral and dorsal rami. Only myelinated fibers can be seen in the ventral root. Figure 2 shows a bundle of fibers, which can be followed from the ventral root, partly surrounded by fibers from the dorsal root running in another direction. The contrast between the fibers from the two sources is striking. Bundles of fine, darkly staining, unmyelinated fibers are seen only among those coming from the dorsal root.

In order to avoid confusing sensory unmyelinated fibers with those of sympathetic origin, it is necessary to study preparations from which the latter have been removed by degeneration. In six cats I removed the right abdominal sympathetic chain from the diaphragm to the pelvis, and killed the animals after periods ranging from thirty-nine to eighty-

11. Dogiel, A. S.: Der Bau der Spinalganglien des Menschen und der Säugetiere, Jena, Gustav Fischer, 1908.

12. Ramón y Cajal, S.: Die Struktur der sensiblen Ganglien des Menschen und der Tiere, Anat. Hefte **16**:177, 1906.

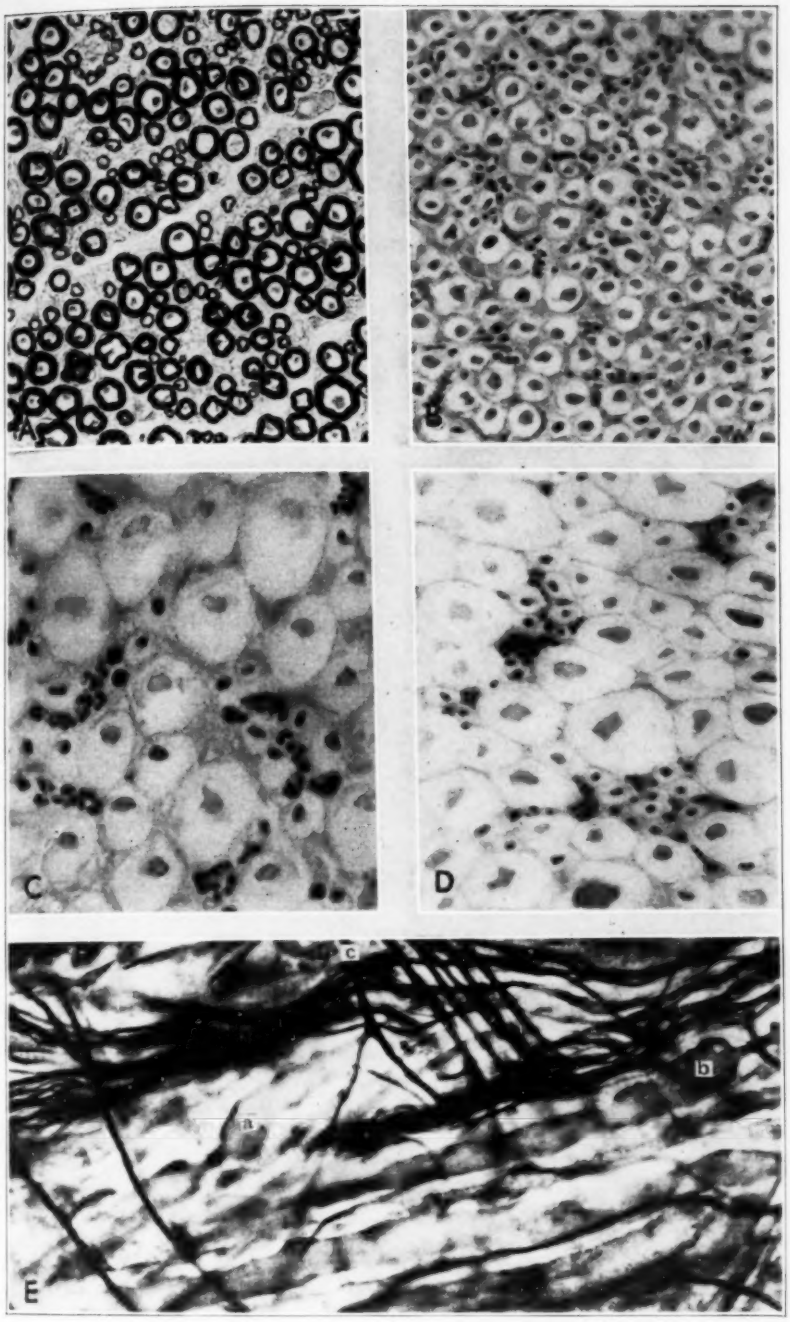

Fig. 1.—*A*, section from a sympathectomized saphenous nerve of the cat stained with osmic acid; × 380. *B*, section from a sympathectomized saphenous nerve of the cat stained by the pyridine-silver method; × 380. *C*, section from a sympathectomized saphenous nerve of the cat stained by the pyridine-silver method; × 750. *D*, section from the sixth lumbar dorsal root of the cat stained by the pyridine-silver method; × 860. *E*, section from a longitudinal section of a spinal ganglion of a dog stained by the pyridine-silver method. The myelin sheaths are unstained. Two myelinated axons (*a*) and (*b*) show constrictions at the nodes of Ranvier. The unmyelinated fibers are much smaller and more darkly stained. One of them (*c*) is seen dividing into two branches of unequal size. The finer branch is directed toward the dorsal root; the coarser branch runs into the nerve. The difference in size of these two branches explains the difference in the diameter of the unmyelinated fibers as seen in the peripheral nerve and in the dorsal root (*C* and *D*); × 650.

four days. The shortest period, over five weeks, was sufficient to allow for the complete degeneration of all of the sympathetic fibers entering the lumbar nerves through the gray rami. For study I selected the saphenous nerve and the nerve to the vastus medialis, representing a cutaneous and a muscular branch of the femoral nerve.

Sections of each nerve were prepared by the osmic acid and the pyridine-silver methods. Figures 1*A* and *B* represent sections of the same fascicle of a sympathectomized saphenous nerve. The myelinated

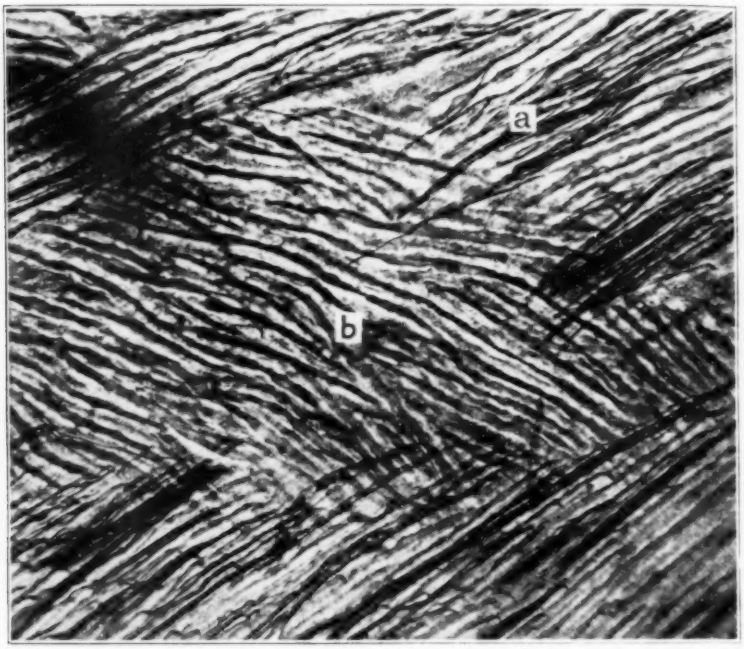

Fig. 2.—Photomicrograph from a longitudinal section of a spinal nerve at the point at which the ventral and dorsal roots fuse to form the mixed nerve; (*a*) dorsal root fibers, (*b*) ventral root fibers. Pyridine-silver stain; × 190.

fibers can be as easily recognized in the pyridine-silver as in the osmic acid preparations, but here the myelin sheaths appear as unstained halos about lightly stained axons. In the interstices among the myelinated fibers are large numbers of unmyelinated fibers. These stain more heavily and are grouped together in bundles. The individual fibers are not differentiated in the photograph, but the bundles are clearly shown, and each contains from three to a dozen or more fibers. These are not bundles of fine myelinated fibers drawn together by the shrinkage of the endoneurium, because accurate counts have been made, and they show that as many myelinated fibers can be recognized in the pyri-

dine-silver as in the osmic acid preparations, and that in addition these bundles of unmyelinated fibers are present (Ranson and Davenport [13]).

Figure 1*C* represents part of a fascicle of the sympathectomized saphenous nerve under a high magnification. The individual unmyelinated fibers appear as black dots and are fairly well differentiated. One can easily satisfy oneself that the dots represent the cut ends of fibers by examining the preparations and varying the focus of the

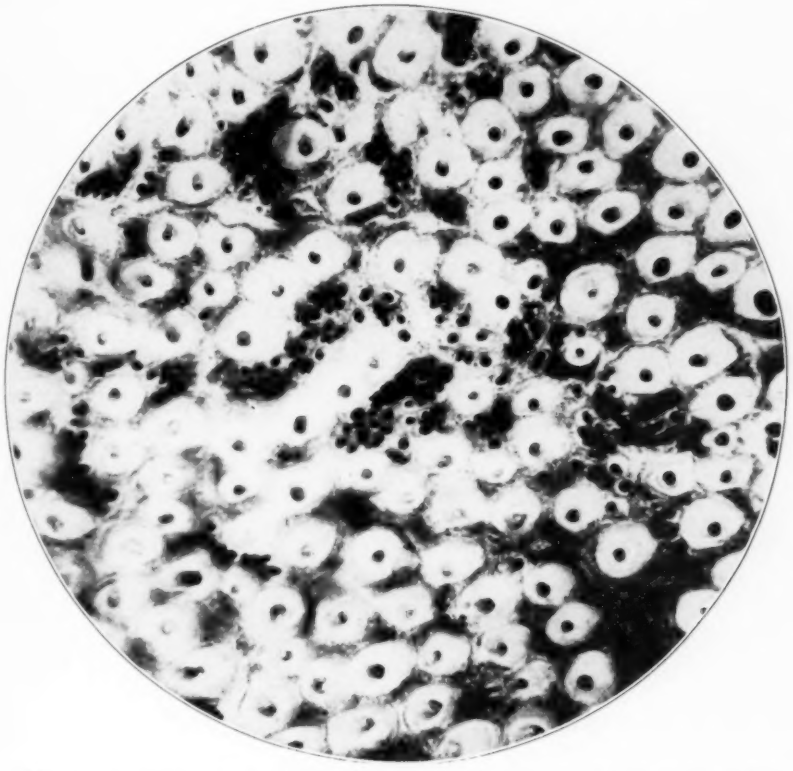

Fig. 3.—Photomicrograph from a human sciatic nerve. Cajal stain; reduced from a magnification of 655.

microscope so as to follow the fibers up through the thickness of the section.

The nerve to the vastus medialis, a purely muscular branch of the femoral, has a different structure. It contains relatively few unmyelinated fibers in preparations from which the sympathetic elements have been removed by degeneration. Differential counts of the axons in these sympathectomized nerves showed a ratio between myelinated and

13. Ranson, S. W., and Davenport, Helen K.: Sensory Unmyelinated Fibers in the Spinal Nerves, Am. J. Anat. **48**:331 (July) 1931.

unmyelinated fibers of 1:04 in the nerve to the vastus, and 1:3.7 in the saphenous nerve (Ranson and Davenport[13]). The unmyelinated fibers in the motor branch probably convey painful afferent impulses from the muscles, since it is known that the sensory fibers for the muscle spindles are myelinated.

Unmyelinated fibers are present in large numbers in the spinal nerves of man (fig. 3), but whether they are relatively as numerous as in the cat remains to be determined. It seems possible that in man a larger proportion of these fine fibers acquire myelin sheaths.

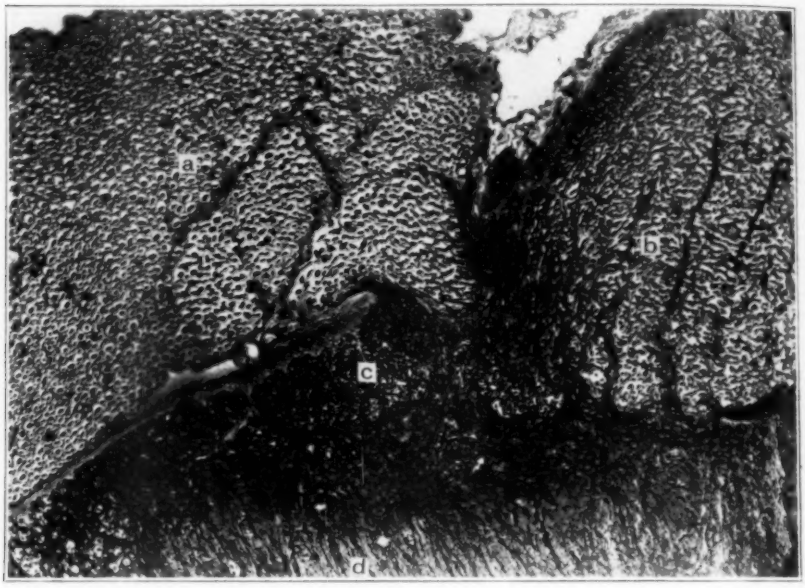

Fig. 4.—Photomicrograph from a section of the sixth lumbar segment of the spinal cord of the cat, showing a fascicle of the dorsal root entering the cord; (*a*) dorsal root, (*b*) fasciculus cuneatus, (*c*) tract of Lissauer and (*d*) substantia gelatinosa rolandi. Pyridine-silver stain reduced from a magnification of 100.

The central branches of the myelinated axons arising from the small cells of the spinal ganglia run through the dorsal root to the spinal cord. They are arranged in bundles of from two or three to a dozen or more (fig. 1*D*). A comparison of figures 1*C* and *D* will show that these fibers in the dorsal root are much smaller than are the peripheral branches of the same axons encountered in the nerve. This is what might be expected from the difference in size of the two branches of the bifurcating axons (fig. 1*E*). In view of their small

size, it is not surprising that Langley [14] was unable to see them in osmic acid preparations of the dorsal roots. The objections that he raised, as well as those advanced by Kiss and von Mihálik [15] and Stöhr,[16] have been considered in another paper (Ranson and Davenport [13]).

Recently Nevin [17] found that there are unmyelinated fibers in the main peripheral nerves that arise in the ganglia of the dorsal roots. They pass mainly to skin branches, but also, in smaller numbers, to muscle branches. The unmyelinated fibers of sympathetic origin travel in peripheral nerves, either free among the larger myelinated fibers or intimately associated with groups of unmyelinated and small myelinated fibers from the dorsal roots. The sympathetic fibers to the skin are more numerous than those to the muscles.

Just before a dorsal root enters the cord, the unmyelinated fibers separate from the myelinated and arrange themselves at the periphery of each small radicle into which the root has divided. In some rootlets they form a thin peripheral zone surrounding the more centrally placed myelinated fibers. As the rootlet enters the cord, the central bundle of myelinated fibers runs over the apex of the posterior horn into the posterior funiculus and the peripherally placed unmyelinated fibers turn laterad into the tract of Lissauer (fig. 4). These unmyelinated fibers are accompanied by a smaller number of very fine myelinated fibers and constitute the lateral division of the dorsal root.

TECHNIC OF STUDIES

The last lumbar and first sacral roots, running as they do parallel to the long axis of the cord, offer especially favorable material for tracing the course of the unmyelinated fibers. The best procedure for demonstrating these bundles of the lateral division of the dorsal root has been as follows: A cat is eviscerated to drain the blood from the tissues, the spinal cord is exposed, and a ligature is passed around the cord and roots at the level of the second sacral segment to hold the roots in close apposition to the cord. The seventh lumbar and first two sacral segments are removed in one block and fixed in ammoniated alcohol for twenty-four hours. The ventral half of the block is sliced away with a razor, and the remainder, including the undisturbed dorsal roots, is put back into ammoniated alcohol for twenty-four hours more. After the usual treatment with pyridine and after thorough washing in water, the piece is rapidly dehydrated, put

14. Langley, J. N.: The Nerve Fiber Constitution of Peripheral Nerves and of Nerve Roots, J. Physiol. **56**:382, 1922.

15. Kiss, F., and von Mihálik, P.: Ueber die Zusammensetzung der peripherischen Nerven und den Zusammenhang zwischen Morphologie und Funktion der peripherischen Nervenfasern, Ztschr. f. d. ges. Anat. **88**:112, 1929.

16. Stöhr, P., Jr.: Mikroskopische Anatomie des vegetativen Nervensystems, Berlin, Julius Springer, 1928.

17. Nevin, S.: Degeneration Changes after Unilateral Lumbar Sympathectomy, with General Observations on the Nerve-Fiber Constitution of Peripheral Nerves and Nerve-Roots, Quart. J. Exper. Physiol. **20**:281, 1930.

in ether-alcohol for a minute, dipped in 3 per cent celloidin, dried for a minute in the air, dropped into 70 per cent alcohol for an hour and then carried down into water from which it is transferred to silver nitrate. It is carried through the remaining steps of the pyridine-silver technic in the usual manner.[18] After having been embedded in paraffin, the block is cut into transverse sections which are mounted serially. The purpose of the celloidin is to fill in the interstices among the dorsal root fascicles and bind them down to the cord, thus giving a block favorable for impregnation with silver.

As the first sacral root passes over the apex of the posterior horn, it is broken up by septums into small radicles. The unmyelinated fibers separate from the myelinated and arrange themselves along these septums, which they follow ventrad into the tract of Lissauer (figs. 5 and 6). These bundles constitute the lateral division of the dorsal root, and they contain, in addition to the unmyelinated fibers, a few fine ones that are myelinated. Figure 7 is a high power photomicrograph showing the fine fibers, grouped along such a septum, with the much larger myelinated fibers on either side. Some of the fine fibers are cut transversely and appear as dots, others in the lower part of the picture are seen running obliquely toward Lissauer's tract.

The tract of Lissauer is composed of fine myelinated and unmyelinated fibers and contrasts sharply with the fasciculus cuneatus and dorsal spinocerebellar tract between which it lies, and which are composed almost exclusively of myelinated fibers.[19] Some of its fibers are of endogenous origin, but many of them are derived from the dorsal roots. Experiments have shown that a large percentage of both myelinated and unmyelinated fibers degenerate in the tract of Lissauer after section of the dorsal roots, and that these fibers ascend in the cord for very short distances, not more than a segment or two, before they end in the gray matter of the posterior horn, probably the substantia gelatinosa rolandi.[20]

Recently, these observations have been confirmed for human material by Ingvar.[21] In man, as in the cat, the unmyelinated fibers separate from the myelinated and form a peripheral layer around the entering root bundle and then turn laterad into the tract of Lissauer. Ingvar found that this superficial zone of fine fibers degenerates early in tabes, and that this is associated with an early degeneration of the unmyelinated fibers in the tract of Lissauer.

---

18. Ranson, S. W.: Non-Medullated Nerve Fibers in the Spinal Nerves, Am. J. Anat. **12**:67, 1911.

19. Ranson, S. W.: The Course Within the Spinal Cord of the Non-Medullated Fibers of the Dorsal Roots: A Study of Lissauer's Tract in the Cat, J. Comp. Neurol. **23**:259, 1913.

20. Ranson, S. W.: An Experimental Study of Lissauer's Tract and the Dorsal Roots, J. Comp. Neurol. **24**:531, 1914.

21. Ingvar, Sven: Zur Morphogenese der Tabes, Acta med. Scandinav. **65**: 645, 1926-1927.

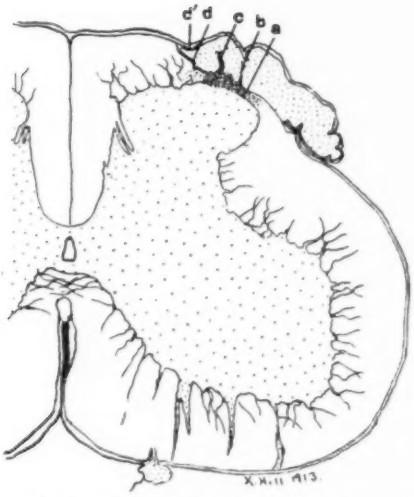

Fig. 5.—Diagram of the septums breaking the first sacral root into small fascicles; (*a*) tract of Lissauer, (*b*), (*c*) and (*d*) septums.

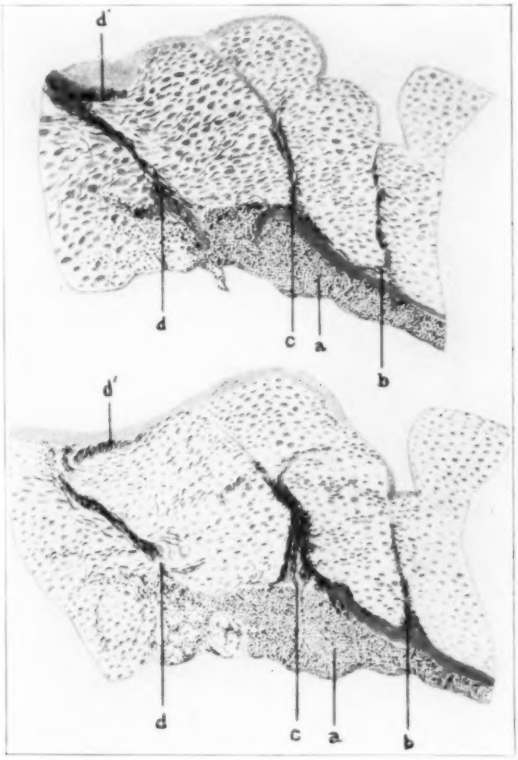

Fig. 6.—Two sections through the dorsal root shown in figure 9. Unmyelinated fibers are seen arranged along the septa (*b*, *c* and *d*) and entering the tract of Lissauer (*a*).

Fig. 7.—Photomicrograph from a section of the first sacral segment of the cat's cord showing a septum separating two fascicles of the dorsal root just before it enters the cord. Unmyelinated axons are arranged along this septum. Pyridine-silver stain; ×740.

It will be evident that the sharp separation of the larger myelinated from the finest myelinated and unmyelinated fibers, as they enter the cord, corresponds to the segregation of the tactile and pain pathways. Tactile impulses are known to ascend for a short distance at least in the posterior funiculus, and this is to be correlated with the fact that only the myelinated fibers of the root enter this funiculus. The fact that the fine myelinated and unmyelinated fibers entering the tract of Lissauer from the dorsal root terminate almost at once in the gray matter suggests that they convey pain and perhaps also temperature sensations, since these impulses are known to pass through the gray matter promptly after entering the cord.

In the first sacral segment of the cat's cord, the bundles of unmyelinated and fine myelinated fibers, which constitute the lateral division of the root, are so placed that they may be easily divided by raising the root and making a very slight cut along the posterior lateral sulcus. A cut of

The Order of Blocking of Sensory Fibers by Cocaine and by Pressure

Cocaine Block		Pressure Block	
Function	Size of Fibers	Function	Size of Fibers
Pain Cold	Small	Motor Touch	Large
Warmth Touch	Medium	Cold Warmth	Medium
Motor	Large	Pain	Small

this sort, which, as shown by subsequent microscopic examination, did not damage the large medial division of the dorsal root through which the myelinated fibers reach the posterior funiculus, eliminated the pain reflexes. Immediately before this cut was made, stimulation of the root caused struggling, a rise in blood pressure and rapid respiration; but after the cut had been made, none of these responses could be elicited. On the other hand, most of the myelinated fibers of the medial division of the root could be cut without preventing these reflexes (Ranson and Billingsley[22]). The inference is clear that pain impulses are conveyed by the fibers forming the lateral division of the dorsal root.

The fibers of this lateral division of the dorsal root are all small, even the few myelinated fibers that it contains are very fine. It is interesting to note that Gasser and Erlanger,[23] working with the cathode ray oscillograph, have furnished conclusive evidence that the fibers that convey pain are among the smallest in the nerve. When cocaine is applied to a nerve, function is not lost all at once, but gradually

22. Ranson, S. W., and Billingsley, P. R.: The Conduction of Painful Afferent Impulses in the Spinal Nerves, Am. J. Physiol. **40**:571, 1916.

23. Gasser, H. S., and Erlanger, J.: The Rôle of Fiber Size in the Establishment of a Nerve Block by Pressure or Cocaine, Am. J. Physiol. **88**:581, 1929.

and in the following order: pain, cold, warmth, touch and motor impulses. Analyses of the action potentials show that with this sort of block the action potentials of the small fibers disappear first, then those of the medium-sized fibers and finally those of the large fibers, as shown in the accompanying table. When a pressure block is applied to a nerve, function is lost in the reverse order: motion, touch, cold, warmth and pain; and in this case the cathode ray oscillograph shows that the fibers are thrown out of function in the order of their size, beginning with the largest. The fine fibers and the sense of pain are the last to be affected by pressure and the first to be affected by cocaine. It is impossible to escape the conclusion that pain is conveyed by the fine fibers.

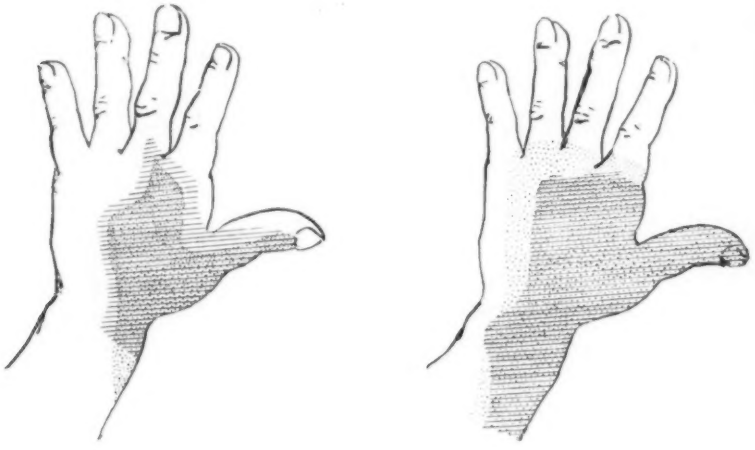

Fig. 8.—Diagram illustrating the sensory dissociation (*A*) resulting from section of the superficial branch of the radial nerve (Head), and (*B*) from section of the fourth to the eighth cervical dorsal roots (Davis). Horizontal lines indicate tactile anesthesia and the stipple, analgesia.

That touch and pain fibers belong to quite different systems is indicated by the sensory dissociations that result from nerve lesions. After section of a peripheral nerve, the area of tactile loss is greater than that of analgesia, indicating that the pain fibers of adjacent sensory nerves overlap more than do those conveying tactile sensibility (fig. 8*A*). After section of the dorsal roots, however, the area of tactile loss is smaller that that of analgesia, indicating that the tactile fibers overlap from one dermatome into the other more widely than do the pain fibers (fig. 8*B*). It is difficult to account for these facts, except on the assumption that pain and touch are mediated by different fibers.

From a study of the nerves of the arm in man and the monkey it has been learned that the median nerve at the wrist, which in proportion to its size supplies a relatively small area of skin richly endowed with tactile sensibility, contains a very high percentage of myelinated fibers and relatively few unmyelinated fibers. On the other hand, the medial cutaneous nerve, which in proportion to its size supplies a relatively large area of skin which is sensitive to painful and thermal stimuli but much less so to touch than are the tips of the fingers, contains a very large number of unmyelinated fibers.[24] From their relative distribution in these nerves one may infer that unmyelinated fibers convey painful, and myelinated fibers, tactile impulses.

How far it is justifiable to draw a sharp morphologic and physiologic distinction between the unmyelinated and the finest myelinated fibers is a debatable question. In the spinal nerves of the cat the distinction seems to be sharp. In transverse sections stained with osmic acid not more than 1 or 2 per cent of the fibers could possibly be regarded as transitional forms. For the most part, the finest myelinated fibers have sharply defined black sheaths, which are entirely different from the light gray, barely visible lines surrounding each of the unmyelinated axons (Ranson and Davenport [13]). Nevertheless, the possibility is recognized that the proportion of sensory fibers that are myelinated may vary in different species of animals, and that there may be relatively fewer unmyelinated fibers in man than in the cat. Owing to the difficulty in securing perfectly fresh material satisfactory for study, the structure of human nerves has not been so carefully studied.

In the trigeminal nerve of the cat unmyelinated fibers are present, but in relatively small numbers. Windle [25] gave a good picture of them in the frontal nerve, and showed that they are much less numerous here than I have found them in the saphenous nerve. Both frontal and saphenous are purely cutaneous nerves, and it is somewhat difficult to understand why the frontal should be so much better myelinated. However, it is undoubtedly true that there are fewer unmyelinated fibers in the trigeminal than in the spinal nerves.

Tactile discrimination is highly developed in certain parts of the trigeminal area—the lips and the tip of the tongue—and is somewhat greater on the forehead than on the arm or leg. But tactile discrimination is largely a matter of perception and cannot be considered an

24. Ranson, S. W.: Unmyelinated Nerve Fibers as Conductors of Protopathic Sensation, Brain **38**:381, 1915.

25. Windle, W. F.: The Distribution and Probable Significance of Unmyelinated Nerve Fibers in the Trigeminal Nerve of the Cat, J. Comp. Neurol. **41**:453, 1926.

altogether safe criterion for judging the density of innervation. A safer basis would be the number of tactile spots per unit area. On this point I have not found accurate information. It is known that in some parts of the trigeminal area, i. e., throughout the oral cavity, pain spots are few. Whether the high percentage of myelinated fibers in the trigeminal nerve can be correlated with a corresponding development of tactile sensibility in the region of distribution of that nerve remains uncertain. The large percentage of fine myelinated fibers in the branches supplying the cornea and the dental pulp is of special interest in this connection.

After removing all of the sympathetic fibers by degeneration, Windle [25] found in the long ciliary nerves only 5.58 per cent of large and medium-sized myelinated fibers, 59.23 per cent of small myelinated fibers and 35.19 per cent of unmyelinated fibers. Since these nerves are at least partially responsible for the innervation of the cornea, which is sensitive to painful stimuli only, the inference may be drawn that pain from the cornea is mediated by small fibers, perhaps both myelinated and unmyelinated. The pulp of the teeth is said to be sensitive to pain and to changes in temperature which are felt as pain, but insensitive to touch; Windle [26] presented evidence that seems to show that the dental pulp is supplied chiefly by small myelinated fibers. In five cats and one dog, he devitalized the teeth by removing the pulp, and found that the majority of the reacting cells of the gasserian ganglion were of the small and medium-sized type that give rise to unmyelinated fibers in the spinal ganglion. The relatively small number of unmyelinated fibers in the trigeminal nerve and the presence of large numbers of fine myelinated fibers in branches supplying the cornea and the dental pulp would seem to indicate that a large number of the fine fibers of the type that are unmyelinated in the spinal nerves have acquired sheaths in the trigeminal nerve. But the rule that pain is conveyed by the sensory fibers of the smallest diameter appears to hold here as well as in the spinal nerves.

Not all of the sensory fibers of the trigeminal nerve bifurcate within the pons into ascending and descending branches. Windle [27] showed by a study of Golgi preparations of the brain of the fetus of the pig that, while most of the coarse fibers divide into a fine ascending branch going to the main sensory nucleus and a thicker descending branch entering the spinal tract of the trigeminal nerve, other fibers, for the most part of fine caliber, turn downward into the spinal tract without giving off

26. Windle, W. F.: Experimental Proof of the Types of Neurones that Innervate the Tooth Pulp, J. Comp. Neurol. **43**:347, 1927.

27. Windle, W. F.: Non-Bifurcating Nerve Fibers of the Trigeminal Nerve, J. Comp. Neurol. **40**:229, 1926.

any branch to the main sensory nucleus. These fibers lie nearer the surface and do not make the sharp bend characteristic of the descending branches of the bifurcating fibers (fig. 9). There is reason to believe that the fine fibers that descend directly into the spinal tract mediate pain and temperature sensations and that the larger bifurcating fibers mediate tactile sensibility. On the assumption that this represents their function, it would be possible for a lesion in the region of the main sensory and motor nuclei and including the bifurcation of the coarse fibers to cause a loss of tactile sensibility without interfering with sensations of pain and temperature (lesion II, fig. 9). This is probably

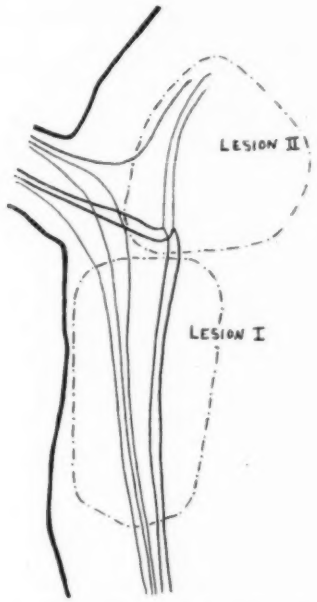

Fig. 9.—Diagram of the sensory fibers of the trigeminal nerve entering the pons, some of which descend without bifurcation into the spinal tract of the tregeminal nerve (Windle).

the explanation of the case described by Spiller [28] in which tactile sensibility was lost on the face, with a paralysis of the muscles of mastication but without analgesia. On the other hand, a lesion in the spinal tract (lesion I, fig. 9) would block the transmission of pain and temperature impulses over the nonbifurcating fibers, but would not prevent the transmission of tactile impulses to the main sensory nucleus over the ascending branch of the bifurcating fibers. Such a lesion is seen characteristically in cases of thrombosis of the posterior inferior cere-

28. Spiller, W. G.: Remarks on the Central Representation of Sensation, J. Nerv. & Ment. Dis. **42**:399, 1915.

bellar artery. Dulling of tactile sensibility, which is sometimes observed in these cases, may be due to the failure of the ascending branch to take over the full function of the bifurcating fiber. Usually, however, after the spinal fifth tract and nucleus have been destroyed as a result of thrombosis of the posterior inferior cerebellar artery, normal tactile sensibility is associated with analgesia and thermanesthesia on the corresponding side of the face. From this syndrome the inference may be drawn that pain and temperature sensibility are mediated exclusively through the spinal tract and nucleus and that that of touch is mediated through the main sensory nucleus of the fifth nerve. This inference was drawn by Spiller [28] and by Winkler [29] apparently independently and simultaneously in 1915, and later by Gerard [30] and Stopford.[31]

Experimental proof that pain is transmitted by the spinal fifth tract was furnished by Gerard in 1923. In the cat this tract was cut just below the bifurcation of the trigeminal fibers. Tracings were taken of blood pressure and respiration. On the normal side, stimulation of the cornea caused a rise in blood pressure and changes in the respiratory rhythm, and these responses, associated as they were with struggling and dilatation of the pupil, may be regarded as pain reflexes. They were entirely lost on the side of the operation. On the other hand, tickling of the nostril caused a sneezing reflex with equal facility from either side of the nose. This may be taken as an indication that tactile sensibility was intact and that of pain lost.

While the cornea was entirely insensitive to pain in Gerard's cats after section of the spinal fifth tract, stimulation of the face with a needle electrode inserted deeply into the tissues still caused pain reactions. But it was found that this held true even after intracranial section of the entire fifth nerve. Davis [32] found that this sensitiveness of the deeper tissues of the face, which persisted after intracranial section of the fifth nerve, was eliminated by a subsequent section of the facial nerve.

It is important to note that the spinal tract of the trigeminal nerve which contains the pain fibers of the trigeminal nerve, is continuous with and has no line of demarcation from the tract of Lissauer, which contains fine myelinated and unmyelinated fibers from the dorsal roots, and that the nucleus of the spinal fifth tract is the direct upward

29. Winkler, C.: A Case of Occlusion of the Arteria Cerebelli Posterior Inferior, Proc. k. Acad. v. Wetensch. Amsterdam **17**:914, 1915.

30. Gerard, Margaret Wilson: Afferent Impulses of the Trigeminal Nerve, Arch. Neurol. & Psychiat. **9**:306 (March) 1923.

31. Stopford, J. S. B.: Sensation and the Sensory Pathway, London, Longmans Green & Company, 1930.

32. Davis, Loyal E.: The Deep Sensibility of the Face, Arch. Neurol. & Psychiat. **9**:283 (March) 1923.

continuation of the substantia gelatinosa rolandi of the spinal cord. All of the available evidence indicates that this column of gelatinous gray substance is the nucleus of reception of the pain fibers in the tract of Lissauer and the spinal tract of the trigeminal nerve.

Windle's diagram of the nonbifurcating fibers of the trigeminal nerve (fig. 9) suggests the possibility that there may be a separation of the pain fibers from the tactile fibers as the trigeminal nerve reaches the pons, the former accumulating near the caudal border of the sensory root. It is possible that this is the explanation of the favorable results obtained by Dandy [33] in tic douloureux after section of the posterior part of the sensory root of the trigeminal nerve near the pons. He believed that the fibers responsible for pain are located in the posterior part of the root, and, on the basis of Windle's work, this is the position in which one might expect to find them.

The sensory fibers for the viscera, which are in the splanchnic nerves, have been isolated by section of the ventral and dorsal roots of the thoracic nerves proximal to the spinal ganglia. In addition to myelinated fibers of all sizes, they include many that are unmyelinated (Ranson and Billingsley [34]). Other unmyelinated fibers from the viscera travel in the vagus nerve (Chase and Ranson.[35]). The nerves to the muscles also contain sensory fibers of this type, though in smaller numbers than do the cutaneous nerves (Ranson and Davenport [13]). Hence, the viscera and muscles as well as the skin are supplied with the fine fibers which I believe mediate pain. Whether these fine fibers are always unmyelinated or whether some of them, especially in the trigeminal nerve, acquire myelin sheaths remains a question for future investigation.

SUMMARY

There are good reasons for believing that pain is mediated by sensory fibers of the smallest diameter. In the spinal nerves of the cat, the majority of these are unmyelinated. In the trigeminal nerve of the cat and in the spinal nerves of man a larger proportion of these fine fibers may have acquired myelin sheaths. It is the fine, nonbifurcating fibers of the trigeminal nerve that carry the sensation of pain from the skin of the face; these descend in the spinal tract of the

33. Dandy, W. E.: An Operation for the Cure of Tic Douloureux, Arch. Surg. **18**:687 (Feb.) 1929.

34. Ranson, S. W., and Billingsley, P. R.: An Experimental Analysis of the Sympathetic Trunk and Greater Splanchnic Nerve in the Cat, J. Comp. Neurol. **29**:441, 1918; The Thoracic Truncus Sympathicus, Rami Communicantes and Splanchnic Nerves in the Cat, ibid. **29**:404, 1918.

35. Chase, M. R., and Ranson, S. W.: The Structure of the Roots, Trunk, and Branches of the Vagus Nerve, J. Comp. Neurol. **24**:31, 1914.

trigeminal nerve, which is continuous below with the tract of Lissauer. These two tracts and the long column of gelatinous gray matter associated with them receive the pain fibers from the skin.

ABSTRACT OF DISCUSSION

DR. ALBERT KUNTZ, St. Louis (by invitation): I have no comment to make by way of criticism, but I wish to express my appreciation of this type of work, and of the contribution that Dr. Ranson has made in pointing out the abundance of these small unmyelinated fibers, particularly in the spinal nerves. I think that the technic that he has to a large extent perfected was an important factor in the study of these small fibers. Technic, doubtless, has played a large part in the study of peripheral fibers, and there are still a few investigators who doubt the occurrence of unmyelinated fibers in the peripheral nerves. One wonders how it is possible to doubt the occurrence of such fibers in preparations such as we saw tonight, and they suggest the importance of the technic that is used. I have been wondering during the concluding portion of the paper whether surgeons will take a clue for the separation of such fine fibers from the larger fibers in the fifth nerve, and modify the operation intended to give relief from the neuralgic pain of the fifth nerve, or whether perhaps a deep operation designed to cut the descending fibers of the spinal fifth tract would be too difficult.

DR. KARL M. DALLENBACH, New York (by invitation): I was asked to comment on the paper from the point of view of an experimental psychologist. I have long been working on the temperature senses and for the past seven years have been engaged in a study of regeneration of the nerves; I am, therefore, much interested in Dr. Ranson's evidence and his conclusions regarding the unmyelinated fibers.

I noticed that Dr. Ranson made the mistake common to many neurologists and physiologists in speaking of "heat" spots. There are, I may dogmatically state, no "heat" spots. There are "warm" spots — independently discovered by Blix in 1883, by Goldscheider in 1884 and by Donaldson in 1885 — which have frequently and mistakenly been referred to as "heat" spots, but there are no heat spots proper. The distinction is not an academic one, but a matter of hard fact. From the point of view of physics, heat is nothing but molecular activity — 0 C., which is usually experienced as cold, is physically 273 degrees of heat; from the point of view of common sense, heat is nothing but a high degree of warmth, merely a step above very warm; but from the point of view of psychology, heat is the name for a quality of experience; it is not molecular activity, not a high degree of warmth, but a unique quality as different from warmth as it is from cold. Curiously enough, however, it is aroused by the simultaneous stimulation of the warm and the cold spots and the fusion of those excitations. For example, if a warm spot is isolated on the skin and is stimulated in any manner whatever, it will give nothing but warmth as long as the stimulus is adequate and is restricted to the isolated spot. If a cold spot is stimulated simultaneously with the warm spot, either normally or paradoxically, the experience of "heat" arises, and that experience is neither warm nor cold. "Heat" is a term that should be reserved for this experience. It is normally aroused by temperatures above from 43 to 45 C. (109.4 to 113.0 F.) that stimulate the warm spots normally and the cold spots paradoxically.

Dr. Ranson's observation that the frontal nerve is composed chiefly of myelinated fibers corroborates his observations in other parts of the body and confirms his general conclusions that pressure is carried by the large myelinated fibers and that warmth, cold and pain are carried by the slightly myelinated or unmyelinated fibers. From the point of view of psychology, one would expect the frontal nerve to be composed of the same kind of fibers as the median nerve that leads to the fingers, for the sensitivity of the areas served by these two nerves is similar. The lips and fingertips have, of the entire body, the highest sensitivity for pressure.

The face, moreover, has a low degree of sensitivity for warmth, cold and pain; indeed, the gums and certain parts of the mouth and cheeks are insensitive to warmth, cold and pain. If Dr. Ranson's correlation is true, the frontal nerve should be composed chiefly of myelinated fibers. That it is composed chiefly of myelinated fibers is a triumphant vindication of his theory.

It was long thought that pain was a matter of general sensitivity; in other words, that the excessive stimulation of any nerve or nerve ending would give pain. This theory was proved untenable in 1896 when von Frey, corroborating Goldscheider's discovery of pain spots, established the specificity of pain and postulated that the function was subserved by free nerve endings. Dr. Ranson's results carried the question of specificity one step further. I cannot see, from the convincing evidence that he presented, how one can escape from his conclusion that the unmyelinated fibers subserve the function of pain.

I wish to raise one more question which is prompted by my interest in the regeneration of nerves: Is there any evidence that the sympathetic system has a peripheral sensory function? I judge from the results that were reported that there is none, yet clinicians, particularly Fraser and Foerster and students of the latter, suggest the possibility. It is tempting to correlate Head's protopathic sensitivity with the sympathetic system, and his epicritic with the sensory system. However, psychologists have never accepted Head's distinction, partly because they could not verify it by introspection, but principally because the experiments of Boring and more recently those of Schäfer did not confirm it. The distinction is untenable, and neurologists are finally following the lead of psychologists in rejecting it. I shall be interested in learning what Dr. Ranson thinks of these matters.

DR. CHARLES A. ELSBERG: Many of us have spent much thought on the problem of the course of the sensory fibers in the peripheral nerves, and of the course of the fiber tracts in the spinal cord and the different modalities of sensation carried by them. If I remember correctly, it was twenty years ago that Dr. Ranson published the first of a series of important studies on this subject, and each paper that has appeared from his pen has been a logical sequence of the one that preceded it. In the first paper Dr. Ranson demonstrated that there are many more fibers in the sensory pathways than were previously known, because there are a much larger number of fine unmyelinated and fine myelinated fibers. However, I still wonder whether there are a sufficient number of fibers to account for all of the varieties of sensation that pass up the nerves and the fiber tracts in the spinal cord. There is so much variation in the disturbance of different sensibilities that it is hard to believe that there are distinct and different fibers for each of these varieties of sensibility. For example, pain is involved sometimes more than temperature, or temperature more than pain; heat is involved sometimes more than cold, and cold more than heat; the sense of position is sometimes involved while the vibratory sense is unaffected, and vice versa.

In Dr. Ranson's second paper he showed that there is a much larger number of fibers with axons in the spinal ganglia than were previously known; he then demonstrated that fine myelinated and unmyelinated fibers travel to the spinal cord through the dorsal roots; this evening he gave the evidence that these fine fibers run in the zone of Lissauer, and that after division of the dorsal roots there is extensive degeneration in Lissauer's zone. Such a degeneration was denied by many previous investigators, but others have found a certain amount of degeneration in this zone. Recently, Ingvar showed that in the early stages of tabes there is a marked degeneration in the zones of Lissauer. Dr. Ranson gave conclusive evidence that the fine fibers that run into the tract of Lissauer are relayed to the substantia gelatinosa, and that these are the fibers that carry sensibility of pain. He gave interesting evidence also with reference to the pain fibers in the trigeminal nerve. He furnished convincing evidence that in the trigeminal nerve near the pons, the pain fibers turn downward into the spinal tract of the trigeminus and end in the spinal nucleus of that nerve, and that the spinal nucleus of the trigeminus is a direct upward continuation of the substantia gelatinosa of the

spinal cord. While the lantern slides demonstrated these facts, the microscopic slides that Dr. Ranson showed me before the meeting portrayed these still more beautifully.

In the early stages of pressure from tumors of the acoustic nerve it is the pain sensation of the cornea that is first involved; this, in accordance with Dr. Ranson's views, can easily be explained as the result of direct pressure on the descending fibers of the spinal tract of the trigeminus. In not a few of the tumors of the eighth nerve, the patients suffer first from severe pain in the distribution of the trigeminal nerve; some patients who presented this condition have even been operated on for supposed trigeminal neuralgia. Dr. Ranson's demonstration that the pain fibers in the trigeminal nerve descend through the spinal tract to the spinal nucleus is suggestive from another standpoint. If he is correct, and I have no doubt of it, then in the future it will be of the greatest importance to examine this part of the trigeminal pathway in the search for a pathologic change in the condition known as trigeminal neuralgia. No careful studies of this part of the trigeminal pathway have ever been made to my knowledge; it may well be that the real lesion, which has eluded us for so many years, is located in this part of the trigeminal pathways. If this theory is true it will perhaps explain some of the claims that, after partial section of the trigeminal nerve in the posterior cranial fossa, facial sensation is preserved while sensibility to pain disappears. If it is possible to divide partially the trigeminal nerve near the pons, then there is no reason why such a section may not in some instances divide only those fibers, the pain fibers that descend to the spinal tract of the fifth nerve. In a patient who has had this operation, tactile sensibility will be preserved in the face, but the patient will be relieved of pain.

Dr. Byron Stookey: Dr. Ranson has long been known for his brilliant anatomic studies, not the least of which is the development of the pyridine-silver stain, which has made possible the study presented this evening. It has also made possible the more recent studies on the degeneration and the regeneration of nerves by Dr. G. Carl Huber of Ann Arbor. Neuro-anatomists and neuropathologists have dealt in the past with a one-sided nervous system, a nervous system made up in large part of medullated nerve fibers. Ranson's stain and his brillant researches with this stain have served to call attention to the important part that non-medullated fibers play in the peripheral and the central nervous system.

The experiments that were reported cover a wide approach and rest on a broad foundation. Dr. Ranson presented in proof of his conclusions morphologic evidence that must be accepted, as well as physiologic substantiation of the morphologic evidence. Finally, he offered clinical confirmation of the deductions that he made. He enabled us to envisage a new morphology and a new mechanism of the peripheral and of the central nervous system. By his studies of the non-medullated fibers he showed that the sensory nonmedullated fibers are derived from the small cells of the dorsal ganglia and that these fibers are relatively richer in those nerves that serve less discriminative functions. Pain is, of course, an affective and not a discriminative form of sensation. Dr. Ranson has further demonstrated that the sensory nonmedullated fibers arrange themselves in a circumferential zone within the rootlets of the dorsal root as this structure is about to enter the spinal cord where in certain instances they may be sectioned without sectioning the medullated nerve fibers. His experiments proved also that at the zone of entrance fine nonmedullated fibers turn laterally to enter the zone of Lissauer and terminate within a segment or two.

Until Ranson's work of a number of years ago, one knew only of the fine medullated fibers forming the lateral branch of the medullated fibers that enter the zone of Lissauer. It was thought that these fibers carried the sense of pain. Dr. Ranson's work has not disproved this fact, but he has shown that pain is carried by a much larger number of fine nonmedullated fibers, the existence of which was previously unknown.

Lissauer's tract was long associated with pain fibers. Ranson showed that the nonmedullated fibers largely serve this function and that in the peripheral nerves

from the periphery to Lissauer's tract a large number of nonmedullated fibers are to be found whose function is the transmission of pain.

It is interesting that the median nerve and the trigeminal nerve, which serve regions requiring instant recognition of painful stimuli, are relatively poorly endowed with fine nonmedullated fibers. These two areas and the nerves serving them should be elaborately supplied with pain fibers. Physiologically, at least, it has been demonstrated that these regions are extremely sensitive to painful stimuli and that they also are capable of a high degree of discriminative sensibility. This is to be expected if one considers the function of the trigeminal nerve in relation to the hairs about the mouth, which in some forms of animals are used as feelers serving important tactile discriminative sensations.

The function of the fine medullated fibers that pass laterally into the zone of Lissauer has not been determined experimentally. Can it be that they serve temperature sense? The work of Gasser and Erlanger indicated a considerable difference in the action potentials for heat as compared with pain, and it may well be that temperature has its own set of fibers. Within the spinal cord, pain may be lost without a lowering of the temperature and temperature may be lowered without a loss of pain, as has long been known clinically, and as has been shown by my own work on differential section of the lateral columns of the spinal cord in chordotomy for relief from pain.

Dr. Kuntz has made the suggestion that instead of cutting the dorsal trigeminal root by the usual subtemporal route, a suboccipital craniotomy and a transverse section into the descending spinal fifth tract may be done. This is a major operation of considerable magnitude, especially since section of the dorsal root is frequently done in elderly patients.

The suggestion has been made that the location of the lesion in trigeminal neuralgia may reside within the spinal fifth tract. Were that true, cutting the nerves peripheral to the lesion would not abolish the pain. It has been an axiom of nerve physiology that section must be done central to the lesion if the painful impulse is to be abolished. Therefore, since section of the dorsal root abolishes pain in trigeminal neuralgia, it would hardly seem plausible to consider the lesion as central.

DR. S. W. RANSON: I am hesitant to make any statements about the application to surgery of the facts that I have presented. It would probably be possible to relieve trigeminal neuralgia by section of the spinal fifth tract as Dr. Kuntz has suggested, but it would probably be a more serious operation than section of the sensory root. Whether or not, as was intimated by Dr. Elsberg, it might be possible to interrupt the pain fibers in the trigeminal root at the point where it enters the pons, cutting merely the caudal border of the root, and so perhaps catching the pain fibers as they swing downward into the spinal fifth tract is worthy of consideration. Ever since I heard that Dr. Pandy was performing operations of this kind, I have thought that his results might possibly be explained on the basis of this superficial course of the fine fibers of the trigeminal nerve in the pons.

I accept the criticism that Dr. Dallenbach made about my use of the word "heat." I should have said "warm spots" because, as he has conclusively shown in his papers, heat is a fusion of different sensory elements. Warmth is a pure sensation.

As an explanation of the fact that the frontal nerve is better myelinated than the saphenous nerve, the suggestion has been made that this may be associated with the rich tactile supply of the trigeminal area. The trigeminal nerve supplies the head, which is used to feel the way as the animal goes forward through the dark. Even in man, the forehead is highly sensitive to tactile stimuli, although the hands have almost entirely replaced the head for feeling out his surroundings. May not this sensitiveness represent a vestige of ancestral heritage, a survival from the time when our ancestors walked on four legs and used the head instead of the hands in gaining impressions by the sense of touch?

Dr. Dallenbach raised a question about protopathic sensibility and two distinct types of fibers. I recognize that protopathic sensibility is discredited by psychologists and neurologists, and therefore I avoided bringing up that subject. If, however, it should prove that there is anything whatever in Head's view, then the separation of sensory fibers into two histologically distinct groups would furnish an organic basis for Head's two types of cutaneous sensation.

Professor Elsberg raised the question of the specificity of the fibers for the different modalities of sensation. If one takes all the different sensory perceptions into consideration, there is really an infinite number of different factors; certainly not all of these can be explained on the basis of specific fibers. I believe, however, that the primary sensory qualities, pain, touch, warmth and cold, which have their specific cutaneous end-organs, have separate conductors in the peripheral nerve.

The work of Ingvar has been mentioned a number of times. Ingvar was able to confirm on human material much of what I told you. He found that the unmyelinated fibers separate from the myelinated and arrange themselves on the periphery of the entering bundles of fibers of the dorsal root and then make their way into the tract of Lissauer, and that in tabes this superficial zone of unmyelinated fibers degenerates early; this early degeneration of the superficial fibers is associated with the early degeneration of the unmyelinated fibers in Lissauer's tract. Hauptmann was inclined to attribute to this early involvement of the superficial zone of unmyelinated fibers the early appearance of pain and analgesia in tabes.

As to Dr. Stookey's question, the small myelinated fibers of the lateral division are intimately associated with the unmyelinated fibers, and therefore there is lacking any very specific evidence, either on the basis of their peripheral distribution in the nerves or their course in the dorsal root, or on the basis of any experimental separation by cutting, that would enable one to say what definite part these fine myelinated fibers play. I think that the possibility that they may carry temperature sensibility is to be taken into consideration. As to the myelinated fibers in the spinal fifth tract, there are of course large numbers of them, and the spinal fifth tract is better myelinated in the upper part of the medulla than in the lower part. If one follows a series of sections of the human brain stem, one sees the fibers decrease in size and in relative number, and the open spaces increase in size as one follows the fifth tract down. I believe that these descending branches of the coarse fibers carry tactile impulses, and I believe that touch is mediated not only by the main sensory but also by the spinal nucleus, and therefore that when there is a lesion of the spinal fifth tract there may be some dulling of tactile sensibility. I should say that pain and temperature are mediated exclusively through the spinal fifth nucleus and touch through both the main sensory and the spinal fifth nuclei.

CONGENITAL ECTODERMOSES (NEUROCUTANEOUS SYNDROMES) IN EPILEPTIC PATIENTS*

PAUL I. YAKOVLEV, M.D.
AND
RILEY H. GUTHRIE, M.D.
PALMER, MASS.

There are congenital malformations affecting more or less electively the ectodermal structures, i. e., the nervous system, the skin, the retina, the eyeball and its contents; sometimes visceral organs are also involved. As these congenital malformations, in many instances, are associated with mental defect and with epilepsy, we thought that such cases deserve to be studied as a special group. As we realize the difficulties inherent to a subject that involves the most intricate problems of embryology and developmental histopathology, we shall limit ourselves to the presentation of a series of case records, and, on the ground of arguments derived from the literature and supported by our own clinical observations, we shall make tentative suggestions. These will include considerations as to the nature of these neurocutaneous syndromes, their mutual relationship and their relationship to the associated neurologic and psychic manifestations, i. e., epilepsy and mental defect.

Three types of neurocutaneous syndromes especially attract attention because of their relative frequency among epileptic patients and also because of the characteristic clinical pictures they present: (1) Recklinghausen's neurofibromatosis; (2) Bourneville's tuberous sclerosis; (3) angiomatosis of the brain, with nevi of the skin in the trigeminal area.

We shall discuss each of these three types of neurocutaneous syndrome and illustrate them with appropriate cases of our own observation.

RECKLINGHAUSEN'S NEUROFIBROMATOSIS

Recklinghausen's neurofibromatosis, described in 1882 by von Recklinghausen,[1] attracted the attention of subsequent observers from both a clinical and a pathologic standpoint. The clinical syndrome consists

* Submitted for publication, May 10, 1931.

* From the Monson State Hospital.

1. von Recklinghausen, F.: Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen, in Virchow's Festschrift, Berlin, A. Hirschwald, 1882.

of: (1) tumors of the skin, pedunculated or sessile polypi, sometimes flat, soft and usually painless on pressure, (2) tumors developing along the peripheral nerve trunks and (3) pigmented nevi and so-called "café au lait" spots, distributed irregularly over the body in a greater or lesser number.

The neurocutaneous manifestations of Recklinghausen's disease are, however, not exhausted with neurofibromas and pigmentations. The so-called anemic nevi of Vorner (1906) often have been found among other congenital skin anomalies of neurofibromatosis (Schmidt[2]). The anemic nevi are characterized by their pale white color, by their fading away when the skin is pressed with a glass slab and by their standing out more sharply when the normal skin around them is scratched, with resulting vasomotor reaction. They are considered as due to a congenital anomaly of vasomotor nerves causing permanent vascular spasm (Sebastiani[3]). Parkes Weber[4] studied them in connection with telangiectatic port-wine nevi, and he considered both vascular varieties of birthmarks as neurogenic in nature, the latter being the opposite of the former. The vascular telangiectatic or angiomatous port-wine nevi also have been observed in Recklinghausen's disease.

To the original triad of symptoms referred to, it must be added that the condition is often hereditary, sometimes familial; the persons bearing the anomaly almost always show some degree of mental defect. Cases with normal mental development are occasionally met with and usually are cases of late and abortive neurofibromatosis. The abortive form is represented when only one or the other of the principal features of the condition is evident. Thus, pigmented nevi and "café au lait" spots may represent the only features of the condition (Darier); the symptomatology may be reduced to a few small pedunculated polypi on the skin. The distribution of the tumors of the skin and the nerve trunks in the two extreme forms of the condition—the generalized form in which the integument appears to be literally studded with tumors, and the mild form of mere potential neurofibromatosis with a few tumors found here and there on the body—may not show any special or selective topography. On the contrary, in cases of average but well developed neurofibromatosis the distribution of tumors often shows predilection for certain parts of the body. Thus, the tumors are especially common on the cephalic and caudal ends of the body (the scalp,

2. Schmidt, H.: Naevus anemicus und Morbus Recklinghausen, Dermat. Ztschr. **55**:209, 1928-1929.

3. Sebastiani, F.: Sul naevus anemicus di Vorner, Gior. ital. di dermat. e sifil. **66**:1499, 1925.

4. Weber, F. Parkes: The Relations of Capillary Hemangiectatic Naevus and Naevus Anaemicus to the Nervous System, Brit. J. Dermat. **41**:221, 1929.

face, back of the neck, gluteal fold, groin, perineum and lumbosacral region); then on the shoulders, arm pits, back and thighs. They are less common on the ventral aspect of the trunk; they usually diminish in number toward the distal segments of the extremities, and they are exceptional on the hands and feet. In some cases the number of tumors in the different areas of the body appears to be in direct relationship to the number of metameres composing the respective areas. A good example of such relationship will be given later (case 1). Behind these topographic features of neurofibromatosis an embryogenic principle seems to be at work. The development of neurofibromatosis seems to be facilitated on the cephalic and caudal ends of the neural tube, possibly in relationship to the process of folding and of the differentiation of embryonal sheets, particularly critical in these areas. The further away from the dorsal groove, the less frequent are the tumors, thus suggesting that the origin (anlage) of neurofibromatous tumors is related to the epiblast or to the neural tube.

Sometimes the cutaneous anomaly is present at birth and remains stationary throughout life, or grows further with the development of new tumors and pigmented spots and an increase in size of those already existing. More often, however, the condition begins during childhood and puberty.

From the standpoint of clinical evolution one might discriminate with Schulmann and Terris[5]: (1) stationary forms; (2) subacute forms, with exacerbations and remissions in the growth of tumors; (3) acute forms with rapid development of a generalized neurofibromatosis, the most striking example of which is a case reported by Pierre Marie and Couvelaire,[6] in which the condition developed in a fortnight, and led to death in cachexia; (4) malignant forms, with sarcomatous degeneration of tumors and metastases.

The feature of particular importance to our subject is that the neurofibromatosis of the skin and peripheral nerve trunks is often associated with pathologic changes in the central nervous system, the meningeal envelopes, the roots of the cranial and the spinal nerves and the sympathetic ganglia. An example of such widespread involvement of the nervous system has been described recently by Penfield and Young.[7]

---

5. Schulmann, E., and Terris, E.: Les formes évolutives de la maladie de Recklinghausen, Rev. neurol. **1**:181, 1927.

6. Marie, Pierre; and Couvelaire, A.: La neurofibromatose généralisée, N. iconog. de la Salpêtrière **13**:26, 1900; quoted by Schulmann and Terris (footnote 5).

7. Penfield, W., and Young, A. W.: The Nature of von Recklinghausen's Disease and the Tumors Associated with It, Arch. Neurol. & Psychiat. **23**:320 (Feb.) 1930.

With regard to the histopathology of these changes, the multiplicity and the sometimes radical divergence of opinions indicate that much more light on the subject is needed. Since the first studies of Virchow (1863), the studies of Verocay, Bielschowsky,[8] Pick and Bielschowsky,[9] Lhermitte, Bielschowsky and Rose,[10] Penfield, Penfield and Young [7] and others mark the progress of the histopathology of Recklinghausen's disease. Certain points seem to meet with a more general agreement. The histogenetic basis of Recklinghausen's disease in a broad sense of this term seems to be a congenital malformation of the ectodermal tissues, nerve cells, glia cells, cells of the ependymal layers lining the ventricles and cerebrospinal canal, choroid plexus, cells of Schwann's sheaths, sympathetic ganglia and endings of the sensory nerves in the skin. On the background of the ectodermal malformation develops a hyperplasia, and sometimes a new growth composed mostly of mesodermal tissues. Of the latter, two are particularly important: (*a*) the overgrowth of the elements of fibrous connective tissue—fibroblasts—especially in tumors of the peripheral nerves and in the skin polypi (neurofibroblastoma), and (*b*) the hyperplasia of blood vessels, especially in the central nervous system. This vascular hyperplasia sometimes acquires such a development that areas so affected may be considered as hemangioma.

The process of primitive glial proliferation in the central nervous system has been studied especially by Bielschowsky and his collaborators. This might be described as a gliomatosis scattered throughout the brain and spinal cord, or as a diffuse gliosis. The glial elements in such areas exhibit features of abnormal or defective development of the primitive glia cells—spongioblasts. These glia cells sometimes reach an enormous size and are described as giant glia cells. The vascular hyperplasia with gliosis in the central nervous system is sometimes associated with the formation of cystic cavities, creating a picture of syringomyelia when in the spinal cord or medulla (Lhermitte and Cornil [11] and d'Antona [12]), and when limited to the cerebellum the patho-

---

8. Bielschowsky, M.: Beiträge zur Histopathologie der Ganglienzellen, J. f. Psychol. u. Neurol. **18**:513, 1912.

9. Pick, L., and Bielschowsky, M.: Ueber das System der Neurome und Beobachtungen an einem Ganglioneurom des Gehirns (nebst Untersuchungen über die Genese der Nervenfasern in "Neurinomen"), Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:391, 1911.

10. Bielschowsky, M., and Rose, M.: Zur Kenntnis der zentralen Veränderungen bei Recklinghausenschen Krankheit, J. f. Psychol. u. Neurol. **35**:42, 1927.

11. Lhermitte, J., and Cornil, L.: Sur un cas de syringomyélie avec syringobulbie associée à des naevi pigmentaires et vasculaires, Rev. neurol. **2**:903, 1928.

12. d'Antona, D.: Morbo di Recklinghausen con siringomielia genuina, Riv. di neurol. **1**:274, 1928; Rev. neurol. **2**:971, 1928.

logic changes resemble the condition of hemangiomatosis of the cerebellum (Lindau's disease).

The cutaneous manifestations of Recklinghausen's disease, namely, tumors of the skin and pigmented nevi, belong to the same type of ectodermal malformations combined with mesodermal overgrowth, hyperplastic or actually neoplastic. Recently, Masson,[13] in a careful work, using a perfected technic, was able to show that all pigmented nevi are true nerve tumors, developing from the nerve endings in the skin, and he called them nerve-ending neuromas. The nervous nature of the pigmented nevi was alluded to by Soldan [14] as long ago as 1899.

The ocular manifestations of neurofibromatosis must be mentioned. Several cases of palpebral neurofibromatosis have been described recently by Veil [15] and Terrien, Mawas and Veil,[16] and may represent a monosymptomatic form of abortive Recklinghausen's disease. The neurofibromatosis of the eyeball and of its appendages, often associated with buphthalmos, has been studied particularly by Treacher Collins and Batten.[17] A case of neurofibromatosis of the fifth nerve with buphthalmos has been reported by Sutherland and Mayou.[18] Gliosis and gliomas of the retina with optic atrophy are familiar to ophthalmologists. The presence of myelinated nerve fibers in the retina has been described as an early and sometimes only manifestation of Recklinghausen's disease. Recently, van der Hoeve [19] pointed out the occurrence of retinal tumors of characteristic appearance in cases of Recklinghausen's neurofibromatosis. Similar tumors are observed also in tuberous sclerosis. Van der Hoeve proposed calling them phacomas or congenital nevoid tumors.

The malignant degeneration of cutaneous tumors and of pigmented nevi has been reported often (Schulmann and Terris,[5] Lévy and Liber-

13. Masson, P.: Naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**: 447 and 657, 1926.

14. Soldan: Ueber die Beziehungen der Pigmentmäler zu Neurofibromatose, Arch. f. klin. Chir. **59**:261, 1899.

15. Veil, P.: Neurofibromatose palpébro-orbitaire, Presse méd. **33**:1113, 1925; Un nouveau cas de forme fruste de maladie de Recklinghausen à manifestations palbébro-orbitaire, Rev. neurol. **1**:662, 1928.

16. Terrien; Mawas, and Veil: Neurofibromatose palpébro-orbitaire, Rev. neurol. **1**:662, 1928.

17. Collins, Treacher; and Batten, R. D.: Neurofibromatosis of the Eyeball and its Appendages, Tr. Ophth. Soc. U. Kingdom **25**:248, 1905.

18. Sutherland, G. A., and Mayou, M. D.: Neurofibromatosis of the Fifth Nerve with Buphthalmos, Tr. Ophth. Soc. U. Kingdom **27**:179, 1907.

19. van der Hoeve: Signes oculaires dans la sclérose tubéreuse des circonvolutions cérébrales (Bourneville) et la neurofibromatose multiple (Recklinghausen), Presse méd. **33**:933, 1925.

son [20] and Crouzon, Blundell and Kenzinger [21]). In the central nervous system, similar malignant tumorous processes may take place, sometimes as metastases from the tumors of the skin and sometimes as an entirely primary process (melanoblastomatosis). The most striking example of the latter occurrence has been recently reported by Farnell [22] and Farnell and Globus.[23]

The clinical and pathologic delimitations of Recklinghausen's disease, taken in a broad sense, are anything but clearcut. The analogies in the pathologic changes of Recklinghausen's disease and the frequent association of the latter with the symptomatology and pathologic changes characteristic of gliomatosis and angiomatosis of the central nervous system, of syringomyelia and of tuberous sclerosis create mixed or transitional forms between uncomplicated neurofibromatosis and the aforementioned conditions. It seems, therefore, that Recklinghausen's neurofibromatosis belongs to a broad nosologic group of diseases arising from a congenital anlage and showing a predilection for the systems of ectodermal derivation. Thus, the general term of congenital ectodermosis seems to be justified in this condition.

Owing to the congenital character of this neurocutaneous syndrome, its association with epilepsy is of interest. Such association has been reported in a few cases in the literature, but not as often as one would expect. We believe that the scarcity of such association is due to fortuitous circumstances. In a dermatologic survey of about 500 male patients of this institution, in not less than 10 per cent (55 cases), cutaneous manifestations of abortive neurofibromatosis in the shape of multiple skin polypi, pigmented nevi and "café au lait" spots have been recorded. In our opinion, these congenital skin anomalies are relatively more common in epileptic patients than they are in those with other conditions or in normal persons. This has been also the impression of Dr. M. B. Hodskins, derived from his long clinical experience with epileptic patients.

Four cases of neurofibromatosis, generalized and abortive, will illustrate the association of this condition with epilepsy.

REPORT OF CASES

CASE 1.—*History.*—A. R., a man, was admitted to the Monson State Hospital in 1925, and died on Nov. 13, 1926, at the age of 54. The available family history

20. Lévy, G., and Liberson, M.: Récidives d'une tumeur majeure opérée chez une maladie atteinte de neurofibromatose généralisée, Rev. neurol. **1**:225, 1930.

21. Crouzon; Blundell, and Kenzinger: Maladie de Recklinghausen familiale et sarcomatose associée, Rev. neurol. **2**:91, 1925.

22. Farnell, F. J.: Primary Melanoblastosis of the Meninges and Brain, J. Nerv. & Ment. Dis. **72**:165, 1930.

23. Farnell, F. J., and Globus, J. H.: Primary Melanoblastosis of the Leptomeninges and Brain, Arch. Neurol. & Psychiat. **25**:803 (April) 1931.

did not contain any data of medical importance except that one of the brothers had a large tumor of the hairy part of the scalp. The patient had always been considered mentally below par. At 25, he began to have epileptic attacks. The first attacks consisted of a short period of confusion. Later on, convulsions occurred. On admission he was dull and apathetic, and he had a poor memory. He was able to do light work about the wards for a while following admission. Later on, mental failure became more advanced and he became completely inactive, spending his time between his bed and a bench in the day hall.

Physical Examination.—The patient was of rather small stature and looked older than his age. Numerous fibroma molloscum, varying in size from that of a pinhead to that of a pigeon's egg, mostly pedunculated, soft, painless and somewhat pinkish, were disseminated all over the trunk, shoulders, thighs, neck and hairy parts of the head (fig. 1). A large subcutaneous tumor was present on the forehead above the nose. The rest of the face, as well as the hands and feet, were

Fig. 1 (case 1).—Recklinghausen's disease. *A*, neurofibromatosis predominates on the back and in the sacrolumbar region. The tumors are less numerous over the extremities. *B*, the tumors are less numerous than on the back and are limited largely to the trunk.

free from tumors, but on the trunk they could be counted in hundreds; they were especially numerous on the back near the midline, in the lumbosacral region and between the gluteal folds. On the face, neck, forearms and shins there were so-called "café au lait" spots. The blood pressure was 134 systolic and 80 diastolic. There was no evidence of arteriosclerotic hardening of the arterial trunks. The urine showed a trace of albumin. The Wassermann reaction of the blood was negative.

Neurologic Examination.—The patient had a stooped posture; his movements were slow and clumsy; examination of muscle tonus revealed a mild but obvious muscular hypertonia. There was resistance to passive movements. A definite cogwheel sign was present in both upper extremities. When walking he held his

head, trunk and upper extremities somewhat immobile and stiff. This stiffness was especially marked in the right arm and right shoulder (fig. 1). The tendon reflexes were all present and were hypertonic. The abdominal reflexes were present, and both plantar reflexes were flexor in type. In testing the reflexes of defense, there was observed a complete lack of any emotional or motor protective reaction on the part of the patient. There was no disturbance of sensation. The pupils were contracted; both reacted to light, but sluggishly. Hearing was diminished in both ears. There were no involuntary movements, paralysis or contractures. There were joint deformities of the fingers of the right hand. The habitual posture of both hands when at rest reminded one of paralysis agitans. Pressure along the nerve trunks of the right arm was painful. In November, 1926, bronchopneumonia developed and the patient died. No autopsy was done.

Comment.—This is a typical case of generalized neurofibromatosis. The distribution of the cutaneous tumors deserves special consideration (fig. 1). The tumors were most numerous along the middle area of the back, gradually diminishing toward the ventral midline and markedly decreasing in number on the shoulders and thighs, being absent on the distal parts of the extremities. On the parts of the body composed of many metameres crowded together (trunk, at least 17), there were a greater number of tumors; on the parts composed of metameres more spread out (extremities, from 4 to 5), there were distinctly fewer tumors. Also, the further from the dorsal groove, the fewer tumors were present.

Apart from neurofibromatosis, three features stand in the foreground of case 1: (1) epilepsy since the age of 40; (2) neurologic evidence of a mild akineto-hypertonic syndrome, and (3) progressive mental deterioration. These three elements testify to the involvement of the central nervous system by a diffuse and progressive pathologic process. In the absence of an autopsy, one can say tentatively that the nature of the pathologic process was a diffuse primitive gliosis, or the so-called "central Recklinghausen." The ectodermal character of the disease affecting the skin and peripheral and central nervous system in this case is noteworthy.

Case 2.—*History.*—H. L. M., aged 15, whose father had warts on the face and body which had increased in number and size in later life, and one of whose brothers was feebleminded, was the sixth child in the family. He was born at full term without complications; he was very backward from birth. He did not sit up until 18 months, began to talk at 2 years, and did not walk until 6 years; he was always a bed wetter. At 3 years, he had measles. A month after this illness, the first epileptic convulsion occurred. Since that time he had had convulsions, increasing in severity and frequency, so that at the time of examination he had from six to ten every month. At 8 years, he was admitted to the State School for the Feebleminded, and in 1927, when 12 years of age, was transferred to the Monson State Hospital.

Physical Examination.—The patient appeared to be underdeveloped. The head was somewhat microcephalic, with a sloping forehead. The trunk was pudgy, while the hands and feet were slender. The genitalia were overdeveloped (macro-

genitosomia praecox) and contrasted with the infantile appearance of the patient (fig. 2). There was pronounced asymmetry of the face caused by a soft and mobile tumorous mass, the size of a pigeon's egg, located over the inner angle of the right eyebrow and partially obstructing the right eye. There was a pedunculated, fibromatous polyp, soft and painless, the size of a large bean, above the right elbow, and another on the right side of the back in the lumbar region near the midline. Smaller polypi were present in the intergluteal folds. Several other polypi, varying in size from that of a pea to that of a pinhead, not pedunculated, soft and painless, somewhat pinkish, were scattered all over the body. There were also many pinhead-sized, bluish-red, slightly raised, soft and painless nodules. When the patient was put under a slanting light, the whole skin of the trunk appeared as if covered with slight elevations which were not visible under direct

Fig. 2 (case 2).—The patient at the age of 15, with macrogenitosomia praecox, Recklinghausen's neurofibromatosis, a mental defect and epilepsy (see fig. 3).

illumination. The skin anomalies predominated over the trunk, and were more developed and more numerous over the dorsal aspect of the body than over the ventral aspect. They were absent on distal parts of the extremities.

Neurologic Examination.—There was no evidence of paralysis or contractures. There was no defect in spontaneous voluntary movements. The gait was somewhat awkward, with the feet everted. The tendon reflexes were exaggerated, and the right patellar reflex at times was a bit more active than the left; at times also a few clonic jerks were elicited in the right ankle. The abdominal reflexes were present. The cranial nerves were not affected. The pupils were equal and reacted to light.

Mental Examination.—The patient was an idiot, untidy, unable to dress or undress himself, and gluttonous. He sometimes responded when called by his name, but did not answer questions addressed to him. There was some amount

of articulate speech, but it was void of any psychic content and was merely a verbigeration. Psychomotor activity showed a characteristic monotony, stereotypy and incoherence—slapping of the face, repeated clasping of the hands, grimacing, sometimes swearing and a stereotyped outcry, somewhat like barking.

Laboratory Studies.—Lumbar puncture under general anesthesia showed a relatively high pressure—220 mm. of water—in complete relaxation and in a horizontal position. The spinal fluid revealed nothing of importance; however, the Wassermann reaction was reported as doubtful (?). The Wassermann reaction of the blood was negative. An encephalogram (100 cc. of air) showed dilated subarachnoid spaces, especially in the frontoparietal region, and moderate internal hydrocephalus. The lateral ventricles were moderately dilated. In the region of the pineal gland there were nodular masses that looked like candle gutterings, suggesting calcified tumors of this gland or of the choroid plexus (fig. 3).

Fig. 3 (case 2).—Encephalogram in a case of Recklinghausen's disease with epilepsy from early infancy. The lateral ventricles are dilated, and there are irregular masses behind the thalamus resembling "candle gutterings" and suggesting tumors of the choroid plexus in the region of the pineal gland.

Comment.—Case 2 is an example of an early but already well developed Recklinghausen's disease in a congenital idiot with epilepsy. The presence of multiple warts over the face and body of the father suggests that the condition was hereditary. One brother was feeble-minded. The distribution of the skin anomalies followed the principle mentioned in case 1; namely, the predominance of the small skin tumors over the trunk, especially over the back, and their diminution ventrad and distad; they were absent on the feet and hands. The structure of the body showed congenital developmental deficiency, a microcephalic head, disproportion between the size of the trunk and the slender spindle-shaped feet and hands, and hypertrophy of the genital organs. The latter symptom is interesting in relationship to the roentgen evidence, suggesting tumors in the region of the pineal gland (choroid

plexus). The hypertrophy and premature development of the genital organs are one of the prominent symptoms of tumors in this region of the brain. Noteworthy also is the occurrence of tumors in the cerebral ventricles (choroid plexus) in cases of tuberous sclerosis and in cases of angiomatosis of the brain, as will be discussed later. The whole clinical picture gives a solid ground to accept this case as one of congenital ectodermal malformation, affecting the skin and nervous system, and creating a characteristic neurocutaneous syndrome with epilepsy, mental defect and Recklinghausen's neurofibromatosis.

CASE 3.—*History.*—W. H., aged 54, was examined at the Monson State Hospital on June 28, 1930. In 1928, he had what he called a "breakdown," and for four months, from November, 1928, to February, 1929, was out of work on that account. He was very irritable and depressed, and, "a little thing would ball him up as a child of 2 years." He became very emotional, and it was enough for him to speak of or see something sad to become tearful. He had had some headaches which did not bother him in any unusual way. Up to the age of 52, he was in good health, and claimed that he had had no illnesses to speak of. He was married and had two children, both of whom were in good health. His wife had never had a miscarriage. Since October, 1928, on several occasions he had had "fainting spells," which would begin with a moaning or an outcry. He would fall and usually had no recollection of what had happened. These attacks happened mostly at night, but once or twice during the day. His wife stated that he had convulsive movements during these attacks. Treatment with phenobarbital influenced the attacks favorably.

Physical Examination.—The blood pressure was 140 systolic and 84 diastolic. The patient appeared to be somewhat restless and worried about his condition. When undressed, it was observed that many small pedunculated moles of skin color, ranging in size from that of a pinhead to that of a large bean, were disseminated on the back of the neck, between the shoulder blades, under the axillae, a few small ones on the back, one large one under the left axilla, and another, the size of a large bean, in the intergluteal fold. Besides these pedunculated moles, there were several flat or slightly raised, pigmented moles, ranging in size from that of a dime to that of a pinhead, of chocolate brown color, distributed also mostly on the back. The third variety of skin anomalies consisted of small pinhead-sized, pink telangiectasias on the trunk and upper extremities. The front of the chest and abdomen were free, or practically free, from any of these nevi.

Neurologic Examination.—The eye movements were free; there were a few initial nystagmic movements when looking to the right, which were not persistent. The pupils reacted to light and in accommodation. The eyegrounds showed moderate sclerosis of the retinal vessels. The tongue protruded symmetrically, and the face was symmetrical at rest and during action. The left platysma muscle was somewhat more active than the right. The tendon reflexes were very active in the upper and lower extremities, and the right patellar appeared to be somewhat more so than the left. There was no tremor in the arms or hands. Diadokokinesia was distinctly defective in the left upper extremity, but fairly good in the right. The finger-to-nose test showed mild but distinct intention tremor in the left arm, much less, though also evident, in the right. The heel-to-knee test appeared to be slow in the initiation of movement but otherwise was correct. The abdominal reflexes were somewhat more active on the left than on the right. The

plantar reflex was of the extensor type on the right, and flexor on the left. There was no combined flexion sign, and no Barré sign. The Oppenheim sign was flexor on both sides. The reflexes of defense appeared to be of normal pattern. The tonic postural reflexes were distinctly diminished in the right foot as compared with the left. Sensory examination gave negative results.

Laboratory Studies.—Lumbar puncture revealed an initial pressure of 125; the fluid contained 2 cells, small lymphocytes; globulin, 0; total protein, 61; colloidal gold curve, 4421000000. The Wassermann reaction of the blood and spinal fluid was negative.

Comment.—The epilepsy of late onset, emotional incontinence, extensor response on the right, intention tremor and mild adiadokokinesia, more prominent on the left side, horizontal nystagmus on looking to the right, high total protein in the spinal fluid, and the colloidal gold curve of low dementia paralytica type, with the negative Wassermann reaction of the blood and spinal fluid, are suggestive of multiple sclerosis. However, such a diagnosis has a serious drawback in the systematized character of the neurologic syndrome, pointing to a focal lesion above the medulla rather than to a disseminated lesion of the central nervous system. Also, the age of the patient is somewhat uncommon for the beginning of the first manifestations of multiple sclerosis. The skin manifestations of Recklinghausen's neurofibromatosis are of a nature to make one especially cautious in accepting the diagnosis of multiple sclerosis. A primitive gliosis of the central nervous system (central Recklinghausen) may be responsible for the symptomatology in this case, and also for the changes in the spinal fluid, especially the high total protein content with a normal cell count. Whatever the exact nature of the condition, we are inclined to believe that between the neurologic symptoms and the characteristic cutaneous manifestations there is an intimate relationship, the latter being at least the indication of a congenital predisposition of the ectodermal tissues to the disease that became manifest at the age of 50 under the influence of arteriosclerotic changes and possibly other unknown factors.

In this case, also, the skin tumors and birthmarks showed a characteristic distribution on the dorsal aspect of the trunk, on the back of the neck, between the shoulder blades and in the sacro-iliac region, intergluteal folds and perineum, while the tumors were absent on the ventral aspect of the trunk and in the distal segments of the extremities.

CASE 4.—A. C., aged 20, was born at full term; her early development was uneventful; however, at the time when she entered school she was found to be considerably below par mentally. Since the age of 18, she had had epileptic seizures, and on account of epilepsy and mental deficiency (intelligence quotient 52) she was admitted to the Monson State Hospital. Neurologic examination gave no results of particular interest. The face, shoulders, abdomen and thighs were covered with many pigmented spots, the sizes varying from that of a pinhead to that of a dime, some of them hairy, some flat and others slightly elevated.

Comment.—The mental defect, apparently of congenital nature, epilepsy since the age of 18 and pigmented nevi suggest strongly that in this case, also, there is a congenital neurocutaneous syndrome affecting the skin and the central nervous system. The pigmented birthmarks scattered over the integument, as has been already mentioned, may alone represent the syndrome of Recklinghausen's disease. We have referred to the work of Masson which threw much and new light on the pathogenesis of pigmented nevi. These represent true nerve tumors. They are often associated with other symptoms characteristic of Recklinghausen's disease and with pathologic changes in the central nervous system.

Summary.—The neurocutaneous syndrome represented by more or less well developed Recklinghausen's neurofibromatosis, with pigmented nevi and "café au lait" spots, associated with mental deficiency and epilepsy and with other symptoms of involvement of the central nervous system may be considered as clinical manifestations of congenital maldevelopment of ectodermal tissues—a congenital ectodermosis. Epileptic patients, especially with the congenital type, often present evidence of skin anomalies in the shape of polypi, warts, pigmented birthmarks, so-called "café au lait" spots and anemic and vascular (hyperemic) nevi, suggesting abortive forms of Recklinghausen's disease. These anomalies may be considered, in a broad sense, as evidence of a constitutional deficiency arising from a defect in the embryonal development of the ectoderm.

BOURNEVILLE'S TUBEROUS SCLEROSIS (EPILOIA)

Of the three ectodermal or neurocutaneous syndromes under consideration, Bourneville's disease is the most typical and clearcut condition from both clinical and pathologic aspects and the most constant in its association with mental defect and epilepsy. The first descriptions of tuberous sclerosis belong to Bourneville and Brissaud (1880). These were followed by reports of cases and clinicopathologic studies in France and other countries. A complete historical and bibliographic review on tuberous sclerosis was made by Babonneix [24] (1928) in an article to which we refer the reader for further details. In 1911, the English author, Sherlock, proposed the term epiloia for this condition; this term has been adopted by many British writers (Brushfield and Wyatt [25] and Brain and Strauss [26]).

The main elements of the clinical neurocutaneous syndrome of tuberous sclerosis can be summarized in a triad of symptoms: (1)

24. Babonneix, L.: À propos de l'épiloia, Arch. de méd. d. enf. **31**:133, 1928.
25. Brushfield, T., and Wyatt, W.: Epiloia, Brit. J. Child. Dis. **23**:178, 1926.
26. Brain, W. R., and Strauss, E. B.: Epiloia, Recent Advances in Neurology, Philadelphia, P. Blakiston's Son & Company, 1929, p. 348.

multiple warty nodules, sometimes resembling acne rosacea, sometimes like skin polypi, yellowish pink or brownish red, varying in size from that of a millet seed to that of a bean, distributed symmetrically on the face, with a predilection for the sides of the nose, the nasolabial folds, the cheeks and sometimes the forehead and chin (figs. 4, 6 and 7); (2) mental defect; in most of the reported cases the patients were idiots or low grade imbeciles; this condition is found in the four personal observations to be detailed; (3) epileptic seizures, which may be "indistinguishable from those characteristic of idiopathic epilepsy" (Brain and Strauss [26]); however, the fits may vary in their clinical expression (Bielschowsky and Gallus [27]), and jacksonian fits have been reported (Greig [28]).

The condition may be hereditary and familial, but this does not seem to be so common in tuberous sclerosis as it is in neurofibromatosis. Cases have been reported in which hereditary syphilis was evident clinically or serologically in patients or in their parents. Apparently, syphilis may be an important, though scarcely an exclusive, factor in the causation of this syndrome. The condition is a congenital malformation—a germ plasm defect—and on this point agreement seems to be general. The condition, especially the characteristic nodules on the nose and cheeks, is sometimes evident at birth, but usually manifests itself in early childhood or even later. Often other congenital malformations—harelip, cleft palate, spina bifida, microcephaly and additional fingers or toes—are found associated. The warty nodules of the skin on the face are known in dermatologic nosography under the term "sebaceous adenoma" or "naevus multiplex of Pringle" (1891). The term nevus is fully justified, the disease being a congenital structural anomaly of the skin. Jadassohn (quoted by Freund [29]) was one of the first to point out that this anomaly of the skin is neither an adenoma nor a hyperplasia of the sebaceous glands, as it was regarded by Pringle. Later studies have shown no evidence of sebaceous glands in Pringle's nevi in cases of tuberous sclerosis. They consist mainly of a hyperplasia of the connective and vascular tissues; they often arise from the elements of the peripheral glia or Schwann's cells; in other words, they are analogous to the neurofibromas or skin polypi of Recklinghausen's disease (Bielschowsky and Gallus [27]).

The association of the cutaneous manifestations of tuberous sclerosis with those of Recklinghausen's disease is extremely frequent.

---

27. Bielschowsky and Gallus: Ueber tuberöse sclerose, J. f. Psychol. u. Neurol. **20**:1, 1913.

28. Greig, D. M.: A Case of Meningeal Naevus Associated with Adenoma Sebaceum, Edinburgh M. J. **28**:105, 1922.

29. Freund, C. S.: Ueber die tuberöse Hirnsclerose und über ihre Beziehungen zu Hautnaevi, Berl. klin. Wchnschr. **55**:274, 1918.

In four personal cases to be detailed this association is well shown. Often the head, back, shoulders and pelvic region, while less frequently the ventral aspect of the trunk and distal parts of the extremities, bear evidence of other congenital skin anomalies. They are: (1) usually pedunculated skin polypi of varying size scattered over more or less elective areas of the body; (2) raised, though not pedunculated, subcutaneous or intracutaneous nodules, varying in size from that of a pinhead to that of a walnut; (3) areas of fibrous hyperplastic skin, varying in size from that of a half dollar to that of a child's palm, sometimes resulting from an agglomeration of the last mentioned raised nodules, sometimes appearing as a more or less homogeneous thickening of the skin with bluish-white discoloration of the epidermis; (4) pigmented nevi and warts, sometimes covered with hair; (5) "café au lait" spots, and (6) small patches of skin, apparently normal in structure, but remarkable by their clearcut outline, whitish appearance and failure of normal vasomotor reaction (Vorner's naevi anemici). In most examples of well developed "sebaceous adenoma," the skin nodules or warts on the face present two features, one that makes them comparable to the fibroma of the skin, the other characteristic of the telangiectatic (hyperemic) vascular nevi; namely, the nodules appear as acne rosacea and in well developed forms (warts) resemble much the angiomatous nevi of the trigeminal area (Souques, Alajouanine and Mathieu [30]).

At autopsy in cases of tuberous sclerosis, as a rule, are found gross developmental abnormalities and pathologic changes in the brain and other internal organs. Among the latter, tumors and cysts are especially common. The kidneys are particularly often affected and then the heart (C. Demel, 1895); also tumors and cysts in the pancreas, liver, ovaries, etc., are reported. Tumors of the kidney develop almost exclusively in the cortical substance (Hanser [31]); they appear frequently as calcified whitish nodules; however, they may consist chiefly of blood vessels (angioma) or may resemble an adenoma. They are considered as blastomas or congenital tumors.

The pathologic changes in the central nervous system are highly characteristic in both naked eye and microscopic appearance. To the naked eye they appear as nodules of hard consistency and yellowish white, varying in size from that of a pea to that of a quarter, or even larger, disseminated over the surface of the brain. They appear as sclerotic areas along the cerebral convolutions and sometimes have a transversely striated, shrunken aspect. They are surrounded by areas

30. Souques; Alajouanine, and Mathieu: Épilepsie et malformations congénitales de la peau (adenomes sebacés et naevi vasculaires), Rev. neurol. **37**:1127, 1921.

31. Hanser, R.: Nieren- und Herzgeschwülste bei tuberöser Hirnsklerose, Berl. klin. Wchnschr. **55**:278, 1918.

of brain tissue of normal appearance and consistency, so that on palpation of the freshly removed brain one obtains a characteristic impression of hard nodules scattered in the soft cortical substance. After hardening the brain in formaldehyde, this impression is usually lost. The cortex, especially, of the frontal lobes, is the seat of election of these nodules, but they are usually present also in other lobes and in other parts of the brain (Bielschowsky and Freund [32]). Besides nodules characteristic of tuberous sclerosis, there are often found glial and angiomatous tumors and tumorous changes in the choroid plexus. In the choroid plexus the tumorous masses have a characteristic appearance of grapes or "candle gutterings" hanging into the ventricles (see case 2, fig. 3). These tumors are composed of ependymal, glial or vascular elements and, according to the prevalence of one or other of them, are called "ependymoma," "glioma," "angioma" or "angioglioma." Cystic cavities scattered in the central nervous system sometimes are associated with tuberous sclerosis.

The fundamental and classic contribution to the histogenesis of tuberous sclerosis belongs to Pelizzi, who, in a series of studies (1900-1901), has shown that in this condition one is dealing with a profound developmental disorder of cyto-architecture and myelo-architecture of the brain, a condition intermediary between malformation and new growth. To the term of sclerosis given by Bourneville, who regarded this condition as of inflammatory origin, Pelizzi substituted the term of "histio-atypia corticalis disseminata." The work of Bielschowsky marked further progress in the study of the histopathologic changes of tuberous sclerosis. This author has shown that nodules of sclerosis in the brain consist of primitive gliosis, i. e., of abnormal proliferation of undifferentiated or incompletely differentiated primitive glia cells, spongioblasts. He pointed out the intimate resemblance of these glial proliferations to that which one observes in the central nervous system in Recklinghausen's disease, especially the presence of abnormal, rich in plasma, giant cells (Riesenzellen). The glial hyperplasia leads to the destruction of the nerve cells, which disappear in the center of the sclerotic nodules, but increase in number toward the periphery and undergo there a compensatory hypertrophy. Recently, Bolsi,[33] in a contribution to the histopathology of tuberous sclerosis, termed the developmental anomaly "neurospongioblastosis." The nodules are surrounded by areas of nerve tissue, apparently of normal structure; however, heterotopias are often observed. Vascular hyperplasia and sometimes actual angioma were described (Greig [28]).

---

32. Bielschowsky, M., and Freund, C. S.: Ueber Veränderungen des Striatums bei tuberöser Sklerose und deren Beziehungen bei anderen Erkrankungen dieser Hirnteils, J. f. Psychol. u. Neurol. **24**:20, 1918.

33. Bolsi, D.: Contributo all'istologia patologica cerebrale della sclerosi tuberosa, Riv. di pat. nerv. **33**:656, 1928; abstr., Rev. neurol. **1**:126, 1929.

Abortive forms of tuberous sclerosis may be met with. The mental defect in some cases may not be pronounced, the epilepsy may be mild, and the cutaneous manifestations may not be characteristic or reduced to the presence of a few pigmented spots or polypi and a few nodules on the face. In one case reported by Gallus, the only skin manifestation was a fibroma in the region of the knee. A diagnosis of tuberous sclerosis was made and confirmed at autopsy. In another case of abortive tuberous sclerosis reported by C. Jacob, the condition was diagnosed as genuine epilepsy with advanced feeblemindedness. There were found on the back and on the right side of the chest a few small pigmented nevi. Autopsy showed the presence of a typical focus of tuberous sclerosis in the left frontal lobe (quoted after Freund [20]). Aside from mental defect and epilepsy, the clinical manifestations of tuberous sclerosis may be limited to the eyeball and retina—optic atrophy, cataract, retinal tumors or phacomas (van der Hoeve [19]).

In cases of epilepsy and in cases of various forms of constitutional mental defect, the skin must be carefully examined and the ophthalmic examination should not be overlooked, as such examination may lead to an easy and accurate recognition of this neurocutaneous syndrome. The report of four cases will give concrete illustrations of Bourneville's tuberous sclerosis.

REPORT OF CASES

CASE 5.—*History.*—W. E. was a boy, aged 13, whose family history revealed that the father was alcoholic and that the mother died of puerperal septicemia soon after the patient's birth. The Wassermann reaction of the mother's blood taken two days before death, was positive. She had been married twice. By the first husband she had one girl, who is living and healthy. By the second husband she had three children, a girl 16, and a boy 15, both in good health and of average mentality. The third child was the patient.

The patient was born at full term, without complications. No information was obtained as to his development up to 2 years of age. When 2, he was examined at the Boston Psychopathic Hospital. An abstract of the record, which was forwarded to us, states: "Muscularly well developed for a boy of 2 years. Patient could support his weight in standing position but was unable to take a step . . . kept swaying backward and forward, shaking his head, and at the same time making rapid movements with his arms. He made no effort to talk. His attention could not be attracted by external objects. Peculiar shaking of the head was noted . . . the examining psychiatrist felt that the boy was scarcely as well developed mentally as a normal child of 3 months."

At 2 years of age, the patient was committed to the State School for the Feebleminded where he remained until 10 years of age. An abstract from this institution's record states: "Upon admission was suffering from a bad case of weeping eczema which covered the greater part of the right side of his scalp, ear and face. He spends his time in bed or rolling about the sun porch floor, gesticulating in an idiotic manner, sometimes laughing and making a crowing sound. His first epileptic attack recorded by us was in May, 1920, at the age of 3. The physical examination showed lungs normal; heart sometimes shows irregular

action; had history of 'blue spells' for a period of twenty-four hours when 4 years of age. Abdomen negative. Deep reflexes exaggerated. Never walks or talks. Has had chicken pox, measles and whooping cough."

Examination.—In August, 1927, the patient was transferred to the Monson State Hospital where he remained until death on Aug. 5, 1930. On the whole, the examinations of the patient since he came under our observation coincided with the record of the State School. The patient was an idiot, confined to bed. During the daytime, when awake, he was restless, but appeared to be in a state of well-being; he smiled, sometimes laughed, and made groaning noises, sucking his left hand, which he kept deep in his mouth most of the time. Sometimes he sat up, balancing to and fro, or put his legs around his neck, and rolled on the bed in this unusual posture. If approached, and while examined, he yelled and cried; motor agitation increased, and on this account a neurologic examination was difficult.

He could stand on his feet if forced to do so, but he did not walk. He was distinctly underdeveloped in size for his age. The trunk and head were rather large, but the extremities were disproportionately small so that the hands and feet

Fig. 4 (case 5).—The appearance of the patient, who had tuberous sclerosis; nevus multiplex Pringle (sebaceous adenoma).

appeared slender and somewhat spindle-shaped. The right arm showed a mild hemiplegic contracture without actual paralysis. The muscular tonus was diminished; there was laxity of the joints; the legs could be easily brought behind his neck. The tendon reflexes of the upper and lower extremities were exaggerated, more so on the right side. Examination of the abdominal reflexes was not possible. The plantar reflexes were difficult to obtain because of the restlessness of the patient; they appeared to be flexor. The pupils were equal and reacted to light. The patient was not blind, but vision could not be examined. He twitched on a sudden noise. He did not respond when called by name, nor by any other means could his attention be attracted.

Apart from the condition of a mild right hemiplegia with generalized muscular hypotonia, psychomotor hyperkinesia associated with gross mental defect and general somatic underdevelopment, the patient presented characteristic skin anomalies. The face (fig. 4) was covered with typical multiple, yellowish-pink nodules, varying in size from that of a millet seed to that of a large pinhead. These nodules, seated in a somewhat thickened skin, were distributed over the root of the

nose, on both cheeks and on the chin. The rest of the body surface was free from the nodules, but showed other anomalies of somewhat different aspect. In the order of their prominence, these skin anomalies were: (1) small pedunculated tumors, soft and painless, some of them the color of the surrounding skin, others bluish red, varying in size from that of a pinhead to that of a large pea, scattered irregularly over the integument of the neck, but more especially on the back, in the groin and in the intergluteal folds, near the anal orifice; (2) several tumors of the scalp seated deep in the skin, slightly raised; at first glance they could be taken for old scars but differed from these by their somewhat bluish color and

Fig. 5 (case 5).—There are fibromas and a fibrous thickening of the skin in the lumbosacral region and pigmented patches on the back.

by their softness; (3) flat patches of a yellowish color, of cauliflower character, varying in size from that of a pinhead to that of a dime, consisting of minute pedunculated and thickly set skin excrescences; (4) a few dark, not raised, pigmented nevi, of chocolate-brown color; (5) several large, about the size of a child's palm, slightly raised areas of thickened, fibrous, bluish-pink skin, distributed over the dorsal aspect of the trunk, especially the sacrolumbar region (fig. 5); (6) white patches of skin standing out sharper when the skin near them was scratched, and fading away when the skin around them was pressed with a glass slab; there were four over the lower part of the chest, some on the abdomen and several on the back (Vorner's anemic nevi).

Course.—Since November, 1929, the patient had shown an increasing number of convulsions, which ran up to twenty per month; in August, 1930, hypostatic pneumonia developed, and he died on August 5.

Postmortem Examination.—At autopsy, ten hours after death, the skin anomalies on the face were scarcely visible; the face was pale, and only on close inspection could small nodules on the nose and cheeks be noticed. On the contrary, the bluish postmortem discoloration of the skin of the abdomen and the lower part of the chest caused Vorner's anemic nevi to stand out sharper in color and outline.

The pleural cavities on both sides were practically obliterated by adhesions. Both lungs showed intense hypostatic congestion. The heart was small (120 Gm.). The outer wall of the right ventricle contained a soft mass. There were no valvular lesions. The thymus gland was much larger than would be expected in a child of 13 years.

The peritoneal cavity contained a small amount of fluid. The liver was small (610 Gm.), but of normal aspect and apparently of normal structure. The pancreas was grossly lobulated and quite congested; on the cut surface, several petechial hemorrhages were present. The other abdominal organs did not show anything unusual. The left kidney (100 Gm.) was much smaller than normal; it was sclerotic and hard, and its surface was roughened and nodular. Several tumors, the size of a bean, were found in the cortical substance; these tumors were white, homogeneous and hard and crepitated under the knife. The right kidney was much larger than normal (190 Gm.), was dark, of smooth but grossly lobulated surface, and of hard though somewhat resilient consistency. The upper half of the kidney was intensely congested and contained a very vascular mass the size of a hen's egg.

The skull was asymmetrical, the frontal and parietal bones being flattened on the right side. The calvarium was very thick and was detached with great difficulty from the dura. The dura was adherent to the skull along all the sutures of the cranial bones, and along the coronal suture there was a reflection of the dura forming a triangular pocket, opening anteriorly; the dura was thickened but not adherent to the pia. On palpation of the cerebral hemispheres, there was a characteristic impression of hard nodules scattered in the soft cerebral substance. On incision it was found that the convolutions were of abnormal aspect, some of them being unusually wide, as if resulting from fusion of several convolutions; others, on the contrary, were slender and sclerotic. Many of the convolutions were yellowish and had transverse striation; they were of hard consistency and corresponded to the hard nodules felt on palpation through the dura. They were distributed over all the cerebral hemispheres, being most prominent in size and number in the frontal lobe, especially on the right. The cerebellum and brain stem appeared to be free from sclerotic nodules. On a horizontal cut of the brain through the basal ganglia and ventricles, the area of the left striatum showed a hardening similar in consistency to the nodules in the cortex. The lateral ventricles were much dilated, and the choroid plexus was hyperplastic. The spinal cord was of normal aspect.

The brain, spinal cord and specimens of the internal organs and of the skin lesions were preserved for further histologic study.

Comment.—In this observation, both clinical and autopsy observations were typical of tuberous sclerosis. As a point of particular importance to our subject we shall emphasize the association of tuberous

sclerosis with fibroma molluscum and patches of skin fibrosis of characteristic distribution on the scalp and back and in the sacrolumbar region.

After death the hypervascular lesion of the skin of the face ("sebaceous adenoma") became pale and bloodless; on the contrary, the anemic nevi, not distinctly visible during life and requiring special tests to bring them into prominence, became sharper in outline, as these small patches of the skin did not participate in the postmortem discoloration.

It is worthy of note that in this case congenital syphilis was a possible factor in the ectodermal malformation. The mother had a positive Wassermann reaction at the time of the birth of the patient.

Fig. 6 (case 6).—The appearance of the patient, who had tuberous sclerosis or epiloia (nevus multiplex of Pringle). A "sebaceous adenoma" of butterfly distribution can be seen. Note the pedunculated and sessile fibrous and hypervascular polypi, especially in the nasolabial folds and on the forehead.

CASE 6.—*History.*—B. B. was a woman, aged 27, whose maternal grandfather was an inmate in a hospital for mental diseases. The mother was living; she was "nervous" when young, and suffered with "fainting spells." She had had conseven children and one miscarriage; one child died at birth; the other died in vulsions when 1 month of age; the other four were living and well. The patient was the first child, and was born at full term following a dry labor, without instruments. Early infancy was uneventful, but development was retarded. She learned to walk at 18 months; at 2 years she could say only a few words. She had whooping cough at 1½ years, bronchitis at 2, and at 5 years measles with "neuralgia of the head" (?). At the age of 2½ years, she began to have epileptic fits. Her vocabulary remained limited to a few words, and she never learned to talk coherently. Her mental development remained stationary at 1

year. When 10, she was admitted to the State School for the Feebleminded where she remained until she was 17. In 1921, when 18, she was transferred to the Monson State Hospital as an epileptic idiot. The admission record states that the patient did not talk and was destructive and untidy. She had the habit of slapping her face and pulling her hair. She had no paralysis or contractures and no difficulty in walking. Her hands and feet were purple, mottled, cold and clammy. The integument was "covered from head to feet with scars. Over the bridge of the nose and upper portion of cheeks the skin is covered with small naevi, vascular in type."

Examination.—In the last ten years the condition had remained stationary, save for a progressive neurosomatic deterioration. There was evidence of a mild pyramidal paresis on the right, with bilateral extensor response. She had a pronounced muscular rigidity distinctly predominating in the trunk and at the roots of the extremities, diminishing toward the distal segments. The hands and feet appeared to be hypotonic, with diminished tonic postural reflexes, especially in the right foot. She had a bilateral congenital cataract and discriminated only gross differences in light and darkness. The pupils did not react to light; the left cornea had an opacity in the center. The left eye was smaller and more deep-seated as compared with the right. Examination of the eyegrounds was impossible. Otherwise physical examination gave negative results.

The Integument: On the face there was what at first glance appeared to be a hypervascular nevus of butterfly distribution over the nose and cheeks, brownish red in color. On closer examination this nevus consisted of warty fibrous polypi, varying in size from that of a pea to that of a small bean. The polypi were pedunculated and sessile, soft and painless; they appeared to be of a very vascular structure; removal of one for histologic study caused profuse bleeding. The distribution and appearance of these tumors on the face is shown in figure 6. On the periphery of the nevus the skin was covered with pinhead-sized, yellowish-pink nodules; the integument of the extremities seemed to be free from any changes except one typical "café au lait" spot, measuring 2 by 1 inch (5 by 2.5 cm.), over the inner aspect of the left ankle above the malleolus. The trunk was covered with several brownish-yellow or bluish-pink patches of thickened skin of irregular cauliflower appearance, consisting sometimes of thickly set agglomerations of small pinhead-sized polypi. A large, pedunculated, pigmented, soft and painless polyp (fibroma), the size of a cherry, was found in the intergluteal fold near the anal orifice.

Comment.—In this case, mental defect, epilepsy and a characteristic congenital butterfly nevus of the face ("sebaceous adenoma") represent the characteristic clinical triad of the neurocutaneous syndrome of Bourneville's tuberous sclerosis. Skin anomalies were not limited to the face. Patches of fibrosis on the back, pedunculated polypi in the intergluteal fold and a "café au lait" spot on the left leg were associated. The "sebaceous adenoma" of the face exemplified an advanced form of this condition with the formation of sessile polypi with marked vascular hyperplasia, causing a resemblance to certain forms of vascular nevi of the trigeminal area.

CASE 7.—*History.*—W. S., a boy, aged 7, whose family history was without significance, was born at full term without any immediate complications. His further development was defective. He cut his first teeth at 2; he did not walk

until 3, and he never talked. Since the age of 3 months, he had had convulsions. At the time of examination he was able to walk, though he was not very steady on his feet. The greater part of the time he spent in bed or in a chair. He walked only when forced to.

Examination.—He had a large head and a slender, underdeveloped body. The feet and hands were small and somewhat spindle-shaped. He showed no evidence of paralysis or contractures. There was a bilateral extensor response, which was more conspicuous on the left. There were no ocular palsies; the pupils reacted to light and were equal.

The Integument: On admission, four years previous to the writing of this article, he did not show any evidence of skin anomalies, but about one and a half years later a rash developed on the face, of butterfly distribution, consisting of pinkish nodules and resembling acne rosacea. This rash continued to progress, and at the time this article was written it appeared as a typical nevus multiplex of

Fig. 7 (case 7).—The appearance of the patient, who had tuberous sclerosis or epiloia. This is an earlier and more commonly observed form of "sebaceous adenoma" than that shown in figure 6.

Pringle (fig. 7): moreover, on his body, especially on the back, in the sacrolumbar region, and in the groin, one found patches of thickened skin consisting of thickly set, small, bluish-pink or brownish, soft nodules.

Comment.—In this case there is an early form of the neurocutaneous syndrome of tuberous sclerosis. The early manifestations of the characteristic skin changes on the face could be easily overlooked or mistaken for eczema, exanthems, lupus or acne rosacea. Their proper recognition had an obvious diagnostic, prognostic and, therefore, practical importance.

Case 8.—*History.*—N. N., a boy, aged 8, who had one older brother in good health, was born at full term. His childhood was uneventful up to the age of 2 years, when he had measles and had at that time the first convulsion. He recovered from the measles without any immediate complications, but since then his

development had been much retarded. He learned to walk and talk, but appeared as a restless child, noisy and inattentive. Immediately after he had measles a pinkish papular rash was noticed on the face. When 8, he was referred to the Monson State Hospital for observation. His parents with pathetic optimism were convinced that the boy understood much more than he could express and that the proper method of teaching would help him to develop.

Examination.—Examination showed that the patient was an idiot. Neurologic examination gave results of no particular significance. He had no paralysis or contractures. There were no ocular palsies, and the pupils reacted well to light. Speech was articulate, though incoherent, and the vocabulary was very limited. His attention could not be held; he did not answer when called by name, and showed great restlessness.

The Integument: The face was covered with typical yellowish nodules, of butterfly distribution (nevus multiplex Pringle). A few patches of skin fibrosis were found in the sacral region and one small fibroma molluscum in the intergluteal fold. A diagnosis of tuberous sclerosis was made.

Summary.—In this group of congenital ectodermoses represented by the neurocutaneous syndrome of tuberous sclerosis with symmetrical nevus multiplex of Pringle ("sebaceous adenoma") of the face, we emphasize a few points of particular importance.

The other congenital skin anomalies often associated with tuberous sclerosis reveal similarities to Recklinghausen's neurofibromatosis (pedunculated skin polypi, pigmented nevi, "café au lait" spots, Verner's anemic nevi), and at times acquire the characters of vascular nevi of the skin. The "sebaceous adenoma" of the face in particular, in more advanced cases, may resemble both neurofibroma molluscum and vascular nevus.

In their histogenesis all these skin anomalies exhibit the features of congenital tumor formations originating from nerve elements of the skin, combined with hyperplasia of connective tissues and of blood vessels, sometimes assuming the nature of angiomatosis.

The distribution of the skin anomalies shows a specific predilection for certain areas of the body. Pringle's nevus is observed as a rule on the face, in the symmetrical area supplied with terminal filaments of the fifth nerve, and is exceptional below the clavicle. The fibroma molluscum and the patches of skin fibrosis show distinct predilection for the scalp, dorsal aspect of the trunk, and especially the lumbosacral region (intergluteal fold). The distal segments of the extremities usually remain free from the skin anomalies.

The histopathologic changes in the central nervous system show many close analogies, and sometimes are identical with those of Recklinghausen's disease. They consist mainly of primitive gliosis (spongioblastosis), with profound developmental anomaly (histioatypia) and undifferentiation of primitive cells of the epiblast (neurospongioblastosis). The cerebral vascular system and connective tissues, that

is, mesodermal elements, participate in the malformation. Sometimes vascular hyperplasia comes into the foreground, creating actual angiomatosis of the brain and meninges, developing on the background of tuberous sclerosis. The histogenesis of developmental anomalies in the brain, in the peripheral nervous system and in the skin exhibits a remarkable parallelism. In all three the ectodermal malformation is complicated or associated with mesodermal overgrowth. The multiple disseminated character of the lesions, scattered like islands between the areas of normal structure, is characteristic for both changes in the nervous system (nodules of tuberous sclerosis) and for skin anomalies (sebaceous adenoma, fibroma molluscum and patches of skin fibrosis). The cystic formations in the central nervous system (cerebellum), the alterations in the retina (phacoma) and tumors and cysts in the internal organs, especially in the kidneys, contribute to further analogies with Recklinghausen's disease and, as will be shown in the next section, with angiomatosis of the brain.

The malformation affects with a distinct predilection the structures of ectodermal derivation. Tuberous sclerosis is a typical congenital ectodermosis—a neurocutaneous syndrome—associated with mental defect and epilepsy. The developmental anomalies of the ectoblast must, of course, lead to the functional deficiency of ectodermal organs, the nervous system especially as the most differentiated of these organs.

ANGIOMATOSIS OF THE BRAIN WITH VASCULAR NEVI OF TRIGEMINAL DISTRIBUTION

In the characteristic neurocutaneous syndrome consisting of vascular nevi of trigeminal distribution, associated with a neurologic picture of diffuse or focal lesions of the central nervous system, due to congenital vascular malformations, we touch on the most difficult point of our subject. The considerations we present here are merely tentative suggestions made with an intent to set forth an argument rather than to settle a difficult problem. Indeed, the pathology of this vascular neurocutaneous syndrome, at first sight, obviously consists in congenital malformations of the blood vessels—a tissue, not of ectodermal, but of mesodermal, derivation. However, we shall endeavor to bring forward a few arguments that seem to be in favor of the view that the congenital vascular anomaly affecting the skin (port-wine nevi) and the central nervous system (angiomatosis) may be regarded as of neurogenic (ectodermal) origin.

A sweeping generalization of this kind with regard to angiomatosis in a broad sense would be untimely. We have therefore limited our subject to those forms of angiomatosis in which congenital anomalies affect both the skin and the nervous system, carrying with them the

marks of an intimate relationship to the neuromeric segmentation of the epiblast and exhibiting sometimes striking analogies with the clinical and pathologic features characteristic of other congenital neurocutaneous syndromes of much less questionable ectodermal nature, such as neurofibromatosis and tuberous sclerosis.

A brief review of the literature will provide valuable material in support of the view that the vascular neurocutaneous syndrome is a variety among other congenital ectodermoses.

Great interest, especially in recent years, has been aroused in congenital anomalies affecting the vascular system. Apparently there is no structure provided with blood vessels that cannot be the seat of such a vascular anomaly; however, the blood vessels of the nervous system, of the skin, of the retina and also of certain glandular organs seem to be the tissues of election for angiomatosis as compared, for example, to the tissues of nonectodermal origin, such as bone and muscle.

Though familiar to anatomists for a long time, angiomatosis of the central nervous system has attracted special attention since the interesting studies of Lindau[34] (1926). This author, originally occupied with the study of cysts of the cerebellum, came to the conclusion that these cysts arise from congenital blood vessel tumors (hemangioma) of the latter organ. He has shown also that these hemangiogenic cerebellar cysts often (in about 20 per cent of cases) are associated with angiomatosis of the retina (von Hippel's disease) and sometimes with cysts and congenital tumors in the other organs (pancreas, kidneys, liver, suprarenals); moreover, he has pointed out that while the cysts and hemangiomas are commonly found in the cerebellum and often in the medulla and spinal cord, they are only exceptionally, if ever, observed in the cerebrum.

In 1928, Cushing and Bailey, stimulated by the work of Lindau and on the ground of their own experience in the neurosurgery of tumors of the brain, in a paper on hemangioma of the cerebellum and retina[35] and in a monograph on tumors arising from the blood vessels of the brain,[36] made a thorough clinicopathologic study of these conditions. Agreeing with Lindau as to the congenital mesodermal origin of cerebellar hemangiomas, they described them as hemangioblastomas, that is, tumors arising from the primitive endothelium of

34. Lindau, A.: Studien über Kleinhirncysten; Bau, Pathogenese und Beziehungen zur Angiomatosis retinae, Acta path. et microbiol. Scandinav. (supp. 1), 1926, p. 1.

35. Cushing, H., and Bailey, P.: Hemangiomas of Cerebellum and Retina (Lindau's Disease) with the Report of a Case, Arch. Ophth. **57**:447 (Sept.) 1928.

36. Cushing, H., and Bailey, P., Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C. Thomas, 1928.

the blood vessels. They dedicated the first part of their monograph to a study of congenital angiomatous malformations, such as telangiectasias and venous and arteriovenous angiomas, and pointed out that while the angioblastic tumors "proved to be far more common in, if not actually confined to, the cerebellum," on the contrary, "the angiomatous malformations" just mentioned "are more common in the cerebrum than in the cerebellum (the proportion being 14 to 2)." Moreover, in discussing the venous angiomas of the brain, the authors specified that the latter are often associated with vascular nevi of trigeminal distribution.

Lévy [37] (1930) gave an excellent outline of the present status of the problem of angiomatosis of the central nervous system. Two more or less distinct clinicopathologic syndromes can be discriminated in the latter: (1) the neuro-ocular syndrome, in which hemangiogenic cystic tumors of the cerebellum are combined with angiomatosis of the retina (Lindau-von Hippel's disease), and (2) the neurocutaneous syndrome in which vascular nevi of one or several dermatomeres of the skin are combined with the angiomatosis of the respective neuromeres of the central nervous system. However, there is an embryogenic (ectoblastic) link between these two syndromes as the nevoid condition of the retina may occur also in the angiomatosis of the brain, associated with trigeminal nevi.

The nature of the retinal changes in von Hippel's disease caused much controversy, which is of interest to our subject. Certain authors, namely, Lindau, Cushing and Bailey and others, considered that malformation of the blood vessels (capillary angioma of the retina) is a primary process of mesodermal origin, while glial proliferation commonly observed in this condition is a secondary reaction which in some instances may even be in abeyance (Berblinger [38]). On the contrary, Meller and Marburg [39] regarded the glial proliferation as altogether independent—a primary blastomatous ectodermal malformation—and even went so far as to consider angiomatosis as a secondary process (gliosis retinae telangiectodes). Heine [40] followed a somewhat intermediary course between these two opposed views, considering both the glial and vascular processes as parallel, and he spoke of his case of von Hippel's disease as angiogliosis retinae.

---

37. Lévy, G.: L'angiomatose du système nerveux central, Presse méd. **38**:37 (Jan.) 1930.

38. Berblinger, W.: Zur Auffassung von der sogennanten von Hippelschen Krankheit der Netzhaut, Arch. f. Ophth. **110**:395, 1922.

39. Meller, J., and Marburg, O.: Zur Kenntnis des Wesens der sogenannten Czermak-von Hippelschen Netzhauterkrankung, Ztschr. f. Augenh. **66**:1, 1928.

40. Heine, L.: Ueber Angiogliosis retinae mit Hirntumor (capilläres Hämangiom), Ztschr. f. Augenh. **51**:1, 1923.

The solution of this problem seems to be facilitated by recent studies on angiomatosis of the central nervous system, of which the retina is merely a peripheral outgrowth. The histogenesis of vascular malformations as observed in angiomatosis of the central nervous system strongly suggests that in these congenital anomalies, which appear to be of mesodermal origin, there is also an ectodermal element —gliosis—which takes an active part, not as a secondary reaction but as a primitive glial process combined with vascular hyperplasia or even tumor formation. It is this point of view that Roussy and Oberling [41] have advanced on the ground of their studies of angiomatous tumors of the central nervous system. They pointed out that not all hemangiomas are primitive blood vessel tumors, that is, hemangioblastomas in the sense of Cushing and Bailey, or angioreticulomas, as Roussy and Oberling regarded them; but that among these tumors there must be discriminated a group histologically characterized by the coexistence of angiomatosis and primitive gliomatosis. This association may manifest itself either by both processes simultaneously, the result of which is a tumor of complex structure—an angioglioma—or by the separate existence of an angioma and of a glioma or gliosis. The authors pointed out the intimate relationship that can exist between proliferative processes of the neuro-ectodermal tissues and of the vascular (mesodermal) tissues, evident not only in Lindau's disease but also in Recklinghausen's disease.

The two congenital vascular syndromes, the neurocutaneous and the neuro-ocular, seem to be reflecting two different orientations of probably the same congenital malformation; in one orientation the malformation affects mostly telencephalotrigeminal, in the other, metencephaloretinal components of the neural tube. The association with these two syndromes of the visceral angiomatosis might be explained on the ground that the anomaly was of earlier and more diffuse development, involving the lower segmental levels and reflecting itself in respective splanchnomeres. It is worthy of note that in the neuro-ocular syndrome, which seems to be more commonly associated with visceral involvement and which in this way reminds one of similar involvement of the viscera in Recklinghausen's disease, and especially so in Bourneville's disease, one deals with blastomatosis, i. e., true tumor formation from incompletely differentiated embryonal cells; however, in the neurocutaneous syndrome it deals with angiomatous malformation of hyperplastic but not of neoplastic type. This fact strongly suggests that the former congenital malformations—hemangioblastic neuro-ocular syndrome, spongioblastic Recklinghausen's disease

41. Roussy, G., and Oberling, C.: Les tumeurs angiomateuses des centres nerveux, Presse méd. **38**:179 (Feb. 5) 1930.

and neurospongioblastic Bourneville's disease—are of earlier date in the process of embryogenesis than the vascular neurocutaneous syndrome of the encephalotrigeminal variety.

Apart from its ectotropism, i. e., predilection for the structures of ectodermal derivation, a most striking feature of the angiomatosis is the neuromeric distribution of the congenital vascular anomalies. In these features of angiomatosis of the central nervous system are found most conspicuous analogies with the other two types of congenital ectodermoses, i. e., with Recklinghausen's and Bourneville's diseases. A classic example of a vascular neurocutaneous syndrome affecting the spinal neuromere was described by Cobb[42] (1915). In his remarkable case the angioma of the spinal cord, causing a slow compression syndrome (paraplegia), was combined with four small port-wine nevi in the dermatomere corresponding to the neuromere of the spinal cord that was affected with angiomatosis. In a personal communication, Dr. Cobb mentioned another case similar to the one quoted and also a third case of his in which a patient with a vascular nevus of the nasal cavity had a sudden oculomotor paralysis with other acute symptoms of midbrain localization, presumably caused by hemorrhage from an angioma of the midbrain (no autopsy).

The encephalotrigeminal variety of the vascular neurocutaneous syndrome is the most common, and examples of it in the literature are numerous (Cassirer,[43] Lannois and Bernoud,[44] Kalischer,[45] Cushing,[46] Isenschmidt,[47] Oppenheim,[48] Parkes Weber,[49] Dimitri,[50] Marque,[51]

42. Cobb, S.: Haemangioma of the Spinal Cord Associated with Skin Naevi of the Same Metamere, Ann. Surg. **62**:641, 1915.

43. Cassirer, R.: Angiom des Gehirns, Neurol. Zentralbl. **21**:32, 1902.

44. Lannois and Bernoud: Énorme naevus angiomateux de la face avec hémiplégie spasmodique, N. iconog. de la Salpêtrière **11**:446, 1898.

45. Kalischer, S.: Ein Fall von Telangiektasie (Angiom) des Gesichts und der weichen Hirnhäute, Arch. f. Psychiat. **34**:171, 1901.

46. Cushing, H.: Cases of Spontaneous Intracranial Hemorrhages Associated with Trigeminal Naevi, J. A. M. A. **47**:178 (July 21) 1906.

47. Isenschmidt, R.: Die klinische Symptome des cerebralen Rankenangioms, München. med. Wchnschr. **59**:243, 1912.

48. Oppenheim, H.: Ueber klinische Eigentümlichkeiten kongenitales Hirngeschwülste, Neurol. Zentralbl. **32**:3, 1913.

49. Weber, F. Parkes: Association of Extensive Haemangiomatous Naevus of Skin with Cerebral (Meningeal) Haemangioma, Especially Cases of Facial Vascular Naevus with Contralateral Hemiplegia, Proc. Roy. Soc. Med. (Sect. Neurol.) **22**:25, 1929.

50. Dimitri, V.: Tumor cerebral congénito (angioma cavernoso), Rev. Asoc. méd. argent. **36**:63, 1923.

51. Marque, A. M.: Consideraciones sobre angiomas en la infancia, Rev. otoneuro-oftal. **1**:202, 1927.

Brushfield and Wyatt,[52] Aynsley,[53] Laignel-Lavastine, Delherm and Fouquet [54] and Vincent and Heuyer.[55] Cushing [46] described three cases of this variety in which a nevoid condition (angiomatosis) of the brain and cerebral meninges, causing epilepsy, mental defect and paralysis (hemiplegia), was associated with a vascular nevus of trigeminal distribution. The neuromeric character of the congenital vascular anomaly affecting the skin and nervous system was emphasized by Cushing and by Cobb,[42] who followed his master, giving similar interpretations of his case of spinal angioma.

However, while speaking of dermatomeric distribution of vascular nevi, it must be kept in mind that the periphery of such nevi does not always coincide strictly with the boundaries of skin metameres. There often is found some overlapping and sometimes scattering of the port-wine spots over several segments so that it is difficult to correlate the distribution of the nevus on the skin (or mucosa) with a true metamere. It seems possible that the topography of the nevus may be governed by the distribution of sympathetic fibers rather than by embryonal metameres. In the cases with nevi on the trunk (dorsal metameres), these two would approximately coincide, but in the cases with nevi on the shoulders and extremities (cervical metameres) and especially in the nasal-mesencephalic and trigeminal-meningeal-telencephalic cases, the metameric distribution is not clear. Thus, the sympathetic innervation may be the determining factor.[56] The importance of this factor from the pathogenic standpoint will be more fully discussed later.

The predilection of angiomatosis to the cephalic end of the body reminds one of the same principle of the topographic distribution of congenital anomalies observed in neurofibromatosis and in tuberous sclerosis. In the last two neurocutaneous syndromes the skin anomalies were particularly common also in the sacrolumbar region. It is interesting to mention that in a survey of localization of congenital angiomas of the spinal cord, Cobb noted the tendency to the low localizations (lumbar segments, cauda equina).

Lindau (quoted by Kufs), Kufs,[57] Lévy [37] and Roussy and Oberling [41] alluded to the relationship between angiomatosis of the central

52. Brushfield, T., and Wyatt, W.: Hemiplegia Associated with Extensive Naevus and Mental Defect, Brit. J. Child. Dis. **24**:98 and 209, 1927; **25**:96, 1928.

53. Aynsley, T. R.: Hemiplegia Associated with Extensive Naevus and Mental Defect, Brit. J. Child. Dis. **25**:197, 1928.

54. Laignel-Levastine; Delherm, and Fouquet: Épilepsie Jacksonienne par angiome cérébral avec naevus frontal, Rev. neurol. **1**:475, 1929.

55. Vincent, C., and Heuyer, G.: Présentation de deux cas d'angiome veineux cérébral, Rev. neurol. **1**:509, 1929.

56. Dr. Stanley Cobb made illuminating comments on this topic of our subject.

57. Kufs, H.: Ueber heredofamiliäre Angiomatose des Gehirns und der Retina, ihre Beziehungen zu einander und zur Angiomatose der Haut, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:651, 1928.

nervous system, tuberous sclerosis and neurofibromatosis. There are many clinical and pathologic features common to all of them. The cysts and congenital tumors of visceral organs are extremely common in tuberous sclerosis. The visceral neurofibromatosis is well known in Recklinghausen's disease in which tumors of the stomach, ovaries, pancreas, suprarenals, kidneys and sympathetic ganglia are observed. The congenital tumors and cysts in the pancreas, kidney, liver and other organs are often associated with angiomatosis of the central nervous system (von Hippel, Schuback,[58] Kufs,[57] Cushing and Bailey[36] and others). In our case 9, the vascular nevus of the face with angiomatosis of the brain and meninges showed an angiomatous tumor in the lung, and possibly the pancreas was neoplastic, as it was found to be unusually large and lobulated. The tumors of the choroid plexus common in tuberous sclerosis are observed also in Recklinghausen's neurofibromatosis. In our case 2 such tumors were suggested in the encephalogram. They were also found in cases of angiomatosis of the central nervous system (Kufs). In case 9 there was tumorous hyperplasia of the choroid plexus.

The analogies shown by congenital malformations electively affecting the eyeball and retina, common to all three types of neurocutaneous syndromes, offer a particularly suggestive argument in support of the view that angiomatosis of the central nervous system belongs to the group of congenital malformations affecting especially the organs of ectodermal origin. We have mentioned the ocular and retinal manifestations of neurofibromatosis and of tuberous sclerosis in the respective sections; buphthalmos, congenital optic atrophy, glial and vascular proliferations, glioma and congenital retinal tumors of nevoid type (phacomas) are common to both of them. Angiomatosis of the central nervous system also has its ocular counterpart. The buphthalmic condition of the eyeballs in the neurocutaneous syndrome of angiomatosis of the brain with trigeminal nevi is of common occurrence, as has been shown by Aynsley,[59] Brushfield and Wyatt,[52] Parkes Weber[49] and our own observations. Retinal changes of nevoid character (angiomatosis and tumors of the retina) also have been observed; thus, in a case reported by Oppenheim,[48] presenting a trigeminal nevus of the face with mental defect and convulsions, examination revealed the presence of three round tumorous masses in the retina on the side of the facial nevus. In three cases of our own observation to be reported there was at least a strong suggestion that the nevoid condition of of the face was reflected also in the eyeground.

---

58. Schuback, A.: Ueber die Angiomatosis des Zentralnervensystems (Lindausche Krankheit), Ztschr. f. d. ges. Neurol. u. Psychiat. **110**:359, 1927.

59. Aynsley, T. R.: Buphthalmos and Naevus, Brit. J. Ophth. **13**:612, 1929.

Often the association of clinical and pathologic manifestations of these three neurocutaneous syndromes in the same case produces hybrid or transitional forms. In the section on tuberous sclerosis we described cases which illustrate that while the latter condition is commonly combined with cutaneous manifestations of neurofibromatosis, Pringle's nevi of the face often resemble vascular nevi of trigeminal distribution. We have already referred to an extremely suggestive observation of Greig. In this author's patient, an imbecile epileptic with typical "sebaceous adenoma" of the face and right hemiplegia, operation disclosed an angioma of the rolandic area. In a case reported by Gaupp, autopsy revealed "an angioma on the cauda equina measuring 3 x 3 cm.; above this point in the cord were two neurofibromata and a glioma with syringomyelia in which was a fresh hemorrhage" (quoted by Cobb [42]). Recently, Lhermitte and Cornil [11] reported a case of syringomyelia with involvement of the medulla. The patient had a great number of pigmented nevi scattered over the thorax; on the posterior aspect of the trunk there were many "subcutaneous angiomatous dilatations" and near the spinal process of the fourth lumbar vertebra there was an "angiomatous mushroom the size of a small nut." In discussing the case, the authors pointed out that these ectodermal anomalies strongly suggest a malformation of all the ectodermal tissues, including the neuraxis, and they pointed to the frequency with which considerable proliferation of vascular network is found around the cavities of syringomyelia. In 1921, Souques, Alajouanine and Mathieu [30] reported three cases and mentioned two others in which epilepsy and a certain degree of mental defect were associated with congenital malformations of the skin—sebaceous adenoma, vascular nevi of the face and fibroma molluscum. These authors emphasized the importance of the vascular telangiectatic component characterizing the nodules of Pringle's nevus ("sebaceous adenoma") and pointed to the fact that the morphologic aspect of the vascular nevus of the face was comparable to the nodules of "sebaceous adenoma." In connection, they quoted Darier's view that there is no essential difference in the anatomic structure of the vascular nevus and Pringle's "sebaceous adenoma." On these grounds the authors considered the syndrome consisting of epilepsy, mental defect and congenital anomalies, such as vascular nevi of the face and "sebaceous adenoma," as a condition arising from a developmental defect of the primitive ectoderm.

The relationship of vascular nevi to the nervous system was discussed recently by Parkes Weber.[4] Regarding the hemangiectatic or hyperemic nevi as the opposite of the angiospastic or anemic nevi, Parkes Weber quoted Buschke's view that both of these varieties of congenital vascular anomalies might be secondary to a developmental

defect in the vasomotor innervation. Such a view seems to be generally accepted with regard to the pathogenesis of Vorner's anemic nevus. The problem appears to be more difficult with regard to the hyperemic or telangiectatic (port-wine) nevi. However, Laignel-Lavastine and Tinel [60] were able to demonstrate vasomotor paralysis in the vascular nevus in their interesting case. It dealt with an extensive telangiectatic port-wine nevus involving the left side of the neck, left shoulder over the scapula, extending in front to the third rib, involving also the outer aspect of the left arm, left thumb, index finger and part of the dorsum of the left hand. In this case, when both arms were lifted the nevus promptly emptied itself of its blood content, the skin becoming almost normal in color. When both arms were suspended alongside the body, the nevus acquired its port-wine color in from five to eight seconds, while the unaffected extremity returned to normal color only after from fifteen to twenty seconds. A white spot produced by pressure in the nevoid area disappeared in from three to four seconds, while it required from seven to eight seconds before a similar spot disappeared in the symmetrical area of skin of the unaffected extremity. The test of a white streak showed that the idiomuscular contractility of the arterioles in the nevus was exaggerated, as is the case with denervated smooth muscles. The capillary pulse taken in the area of the nevus was almost absent, while it was normal in the respective area of the skin on the unaffected extremity. Thus, the paralysis of vasomotor sympathetic innervation was conspicuous in the area of the nevus; notwithstanding, the other sympathetic functions, such as pilomotor and diaphoretic, were preserved. The authors concluded that they were dealing with a dissociated sympathetic syndrome due to a congenital lesion in the brachiothoracic sympathetic centers of the cord. The distribution of the nevus, the topography of which was not radicular but corresponded with the distribution of sympathetic innervation (A. Thomas), was also in favor of this localization. A similar case of hemangiectatic nevus of pseudometameric distribution, with a dissociate sympathetic syndrome, was reported also by Mativa.[61]

The clinicopathologic considerations just mentioned strongly suggest that in the vascular neurocutaneous syndrome, on the background of congenital malformation of the neuro-ectodermal tissues, there is superimposed a hyperplasia of mesodermal tissues, namely, of blood

60. Laignel-Lavastine and Tinel: Un cas de naevus pseudo-radiculaire de membre supérieur: Contribution a l'étude des topographies sympathiques, Bull. et mém. Soc. méd. d. hôp. de Paris **44**:1048, 1920.

61. Mativa, M.: Naevus pseudo-radiculaire du membre supérieur, Rev. neurol. **2**:796, 1925.

vessels. In our opinion these considerations are important for a deeper insight into the pathogenesis of this syndrome. The pathology of vascular hyperplasia in the brain probably is identical with that of vascular nevi of the skin. The existence of vasomotor innervation of the cerebral blood vessels, since the work of Cobb [62] and his collaborators (Forbes and Wolff), seems to be a well established fact. The congenital ectodermal defect reflecting itself electively on the vasomotor innervation may be looked on as at least one of the factors in the capillary, venous and arteriovenous telangiectatic hyperplasias in the corresponding segments of the skin and in the central nervous system. A congenital defect of such innervation in the brain may lead, therefore, to changes similar to those in the integument. On this ground the angiomatosis of the brain, at least as it deals with angiomatous malformations associated with vascular nevi of trigeminal distribution, may be considered not as a purely mesodermal malformation, which it is from the histogenetic point of view, but rather as an ectodermal malformation of vascular type, "ectodermosis telangiectodes," which it appears to be from a pathogenic standpoint. Such is our main argument, worthy, we believe, of consideration while studying the congenital vascular malformation of the central nervous system, retina and skin.

The association of mental defect and of epileptic fits in cases presenting the vascular neurocutaneous syndrome of encephalotrigeminal type is extremely common. Of course, the presence of one or the other of the elements of the syndrome does not imply necessarily epilepsy or mental deficiency. Indeed, examples are known of persons of great intellectual achievement who were marked with nevi; however, when the congenital vascular anomaly of the facial integument is reflected as well in the central nervous system, the psychic and neurologic evidence of such involvement usually become manifest during early childhood and sometimes at birth. Elmer and Mehlhose regard epileptic fits as an essential manifestation of cerebral angiomatosis (quoted by Cushing and Bailey [36]). Cushing and Bailey are inclined to explain this fact on the ground "that the middle cerebral artery being the most widely distributed of the cerebral vessels, is more likely than the others to be involved in an angiomatous malformation and that the para-central convolutions, in consequence, are prone to be implicated." On our part, we believe that here two factors have to be considered: (1) the cerebral lesion created by the presence of angiomatous malformation and by its complications, hemorrhage in particular, and (2) congenital predisposition created by structural maldevelopment of the brain.

62. Cobb, S.: The Cerebral Circulation: IX. The Relationship of the Cervical Sympathetic Nerves to Cerebral Blood Supply, Am. J. M. Sc. **178**:528, 1929.

Indeed, the vascular anomaly is only a more conspicuous part of the malformation which affects the cerebrum as a whole. The developmental factor we believe is more important in the causation of epilepsy than the subsequent lesion, be it congenital or acquired, vascular or of any other nature. It is the development of functional integration at the higher levels of the central nervous system, gravely compromised at its very root in the course of embryogenesis, that creates the predisposition. The convulsive state in such cases may emerge without any subsequent lesion, or any lesion may bring it out on the predisposed ground. The congenital ectodermoses offer the most concrete examples of constitutional predisposition to mental defect and epilepsy.

We shall report six cases of vascular encephalotrigeminal neurocutaneous syndrome associated with epilepsy and mental defect illustrating this type of congenital ectodermosis.

REPORT OF CASES

CASE 9.—*History.*—F. L., a man, whose family history was unknown, had had epilepsy since infancy and was feebleminded. Since the age of 14, he had been a patient at the Monson State Hospital, where he remained up to death on April 7, 1930, at the age of 40.

Clinical Condition.—The patient was of medium stature and well developed. Previous to admission he had had paralysis of the right side following a series of convulsions. The paralysis improved, leaving a residual hemiplegia with moderate contracture, without atrophy of the extremities. During the time he was in the hospital he had from three to fifteen seizures per month. On the background of a primary mental deficiency, further mental and physical deterioration developed. He was ill tempered, had periods of confusion, and on many occasions showed suicidal and homicidal tendencies. During the last five years of life, he was confined to the ward for demented patients. Apart from right hemiparesis, he presented a typical picture of advanced neurosomatic deterioration; he had a flexion attitude of the head, trunk and extremities, muscular rigidity with cogwheel resistance, exaggerated tonic postural reflexes and hypertonic tendinous reflexes, hypokinesia and lack of emotional reaction to painful stimuli.

The integument was free from birthmarks and other congenital anomalies except that of the face and scalp. The upper part of the face and the forehead on both sides were covered by an extensive vascular, port-wine nevus spreading on both lateral aspects of the head over the scalp into symmetrical areas, resembling the wings of a butterfly (fig. 8). Only the lower jaw and ears were spared by the nevus. Behind the left ear, over the upper portion of the sternocleidomastoid muscle, there was a port-wine nevus the size of a half dollar. The periphery of the birthmark was sharp, though irregular in outline, and a few isolated port-wine spots were present over the forehead and scalp. The central part of the nevus, especially over the nose, eyebrows and upper lip, consisted of thickened hyperplastic skin of rugged appearance, though soft on palpation, resembling cavernous tissue. The eyeballs were large and distinctly protruding. Because of the hyperplasia of the integument, the eyebrows appeared puffy and overhanging, especially the left, which also was disfigured by scars from cuts received in convulsions. Apart from diffuse hyperplastic thickening of the skin in the area of the nevus, there were present, especially on the left side of the face, a few warty

nodules (polypi), soft, but more fibrous in consistency than the rest of the nevus. The photograph of the patient (fig. 8) taken in 1917 gives some idea of the appearance and distribution of the nevus; however, by the time the patient died, thirteen years later, the hyperplastic cavernous appearance of the skin in the area of the nevus became much more advanced, and polypi, especially over the nose and cheeks, increased in size. The pupils were equal and reacted to light. There was a brilliant red reflection of the retinas in both eyes which resembled that of an albino. Ophthalmoscopic examination of the eyegrounds was not made. In April, 1930, the patient suddenly became ill with vomiting and bloody diarrhea, and died within forty-eight hours.

Postmortem Examination.—Autopsy was performed six hours after death. As at that time we were not fully aware of the capital importance of such a case as this, and were not sufficiently informed as to the pathologic peculiarities of angiomatosis in general, the autopsy left much to be desired.

The heart (320 Gm.) did not show evidence of valvular disease or muscular hypertrophy. The left lung (370 Gm.) showed moderate hypostatic congestion,

Fig. 8 (case 9).—Bilateral vascular nevus of trigeminal distribution, sparing the area of mandibular division. Note the hypertrophy of the skin over the nose, cheeks and upper lip, and the fibrous polypi over the face and forehead.

but was otherwise normal. The right lung (520 Gm.) had widespread pleural adhesions and was intensely congested throughout. In the middle lobe there was a spongy mass, the size of an apple, fairly well outlined from the rest of the pulmonary tissue, its consistency being harder than the rest of the lung. When cut through the middle, it appeared as a mass of cavernous tissue filled with blood (angioma). In the center of this mass there was a cavity, also filled with blood. The abdomen, before the incision was made, was distended. The peritoneal cavity contained a large amount of green fluid, with an offensive odor. The transverse colon was much distended and had a black and green mottled appearance. In the splenic flexure of the colon there was a stricture about 5 inches (12.7 cm.) in length. The intestine in this area was only 1½ inches (3.77 cm.) wide, had thick walls and was pale. The lumen was retracted so that only a small finger could be passed. Below the stricture the descending colon was also much distended and dark greenish, appearing gangrenous. In about the middle of the descending colon, on its anterior surface, a perforation was found about

the size of a quarter, round, with thickened irregular black borders. The other parts of the gastro-intestinal tract were not unusual. The liver (1,300 Gm.), spleen (130 Gm.) and kidneys (left, 110 Gm.; right, 190 Gm.) appeared to be normal. The pancreas was large (220 Gm.) and was grossly lobulated; otherwise, nothing unusual was noted; it is possible, however, that a more informed examination would reveal some pathologic change in this organ. The calvarium of the skull was very thick and spongy. On transillumination, bright pink areas in the shape of symmetrical butterfly wings were observed on both sides in the parietal and frontal bones, running from the orbital arches toward the occiput

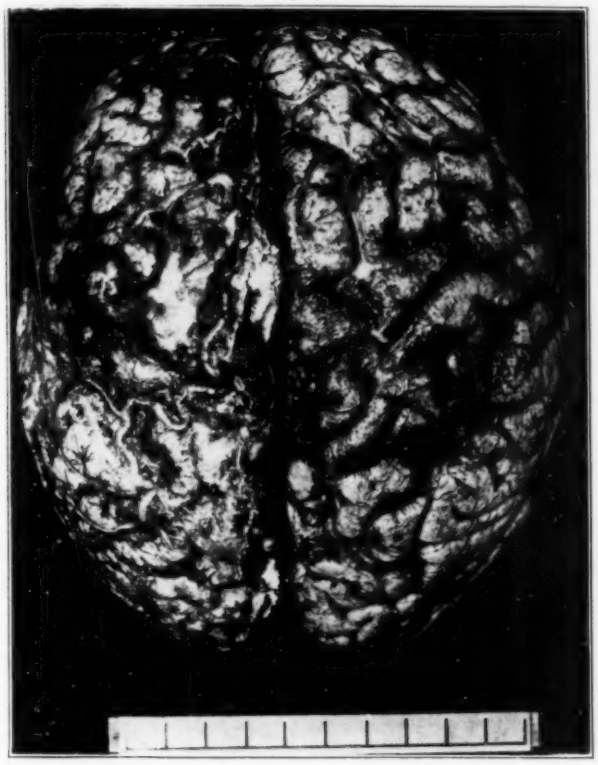

Fig. 9 (case 9).—Angiomatosis of the pial vessels; cortical sclerosis; post-hemorrhagic scars; atrophy of the left hemisphere. (Courtesy of Dr. Myrtelle M. Canavan.)

and practically reflecting in outline the nevus of the forehead and scalp. The dura mater was thick, without evidence of inflammation, and showed blood vessels much increased in number and size, especially in the area of the anterior meningeal artery. This was present on both sides, but was more prominent on the left. The veins were dilated, and small blood vessels were distinctly seen as a fine bluish network all over the hypervascular area covering the frontal and parietal lobes. There were patches of adhesions, especially over the left frontal and parietal surfaces. The left cerebral hemisphere was much smaller than the right, especially the left frontal lobe which was shorter than its mate (fig. 9).

The pial blood vessels showed a distinct increase in size and number. They were thick and tortuous, especially in the left hemisphere, running backward toward the occipital lobe and having the appearance of worms. The convolutions were sclerotic, especially in the left hemisphere, and there was in the cortex a particularly sclerotic, dark area, showing evidence of an old hemorrhagic scar. The brain and cerebellum weighed 1,230 Gm.

The brain, spinal cord, a piece of cavernous mass from the right lung, the area of perforation in the descending colon and a section from the stricture were preserved for histologic study. As we realized the importance of these specimens, we asked Dr. M. M. Canavan to aid us in the further pathologic study of this case, which she consented to do.

Histologic examination of the specimens is not yet completed; however, a few general statements regarding the gross pathology may be made here. The cavernous mass in the lung appeared to be an angioma. The condition of the colon resembled angiomatosis of this portion of the intestine, and the perforation was due apparently to postthrombotic gangrene with hemorrhage. The whole brain was diffusely and intensely hypervascular with a telangiectatic hyperplasia, especially in the area of the sylvian arteries. There was also calcification of the pial and cerebral blood vessels. On the whole, the vascular hyperplasia in the brain, in the meninges and in the skull reflected the distribution of the vascular nevus on the face and scalp. The cerebral ventricles were dilated, and the choroid plexus was very vascular and showed hyperplasia of the tufts. On frontal section, through the optostriatal bodies and cerebral peduncles, the former appeared to be soft and spongy, with many small cavities of softening, especially in the margin of gray nuclei under the white substance of the corona radiata (fig. 10). The cerebellum did not show softening or cysts, though vascularity was much increased to the naked eye. The gasserian ganglia were unusually large, about three times the normal size, and also hypervascular. A pathologic report of this case will be made more thoroughly when the histologic study now under way is completed.

Comment.—The remarkable points in this observation are: (1) the widespread and symmetrical butterfly distribution of a trigeminal nevus involving the area of the two upper divisions and sparing the lower division of the trigeminal nerve; (2) the resemblance of the cavernous warty tufts of the hemangiectatic skin over the nose and cheeks to the nodules of "sebaceous adenoma," such as those in case 6; (3) the resemblance of fibrous polypi in the area of the nevus to those of Recklinghausen's neurofibromatosis; (4) the reflection of the nevoid condition found in the skin throughout the cranial bones, cerebral envelopes and into the brain and choroid plexus; (5) the buphthalmic condition of both eyeballs, with probable involvement of the retinas; (6) angiomatosis in the visceral organs—lungs, large intestine and possibly the pancreas; (7) the absence of true hemangiomatous tumors or cysts in the cerebellum and hindbrain; (8) the hyperplasia of the gasserian ganglia.

On pathologic grounds so far available, the suggestion seems to be justified that this case represents a transitional form between the neurocutaneous and the neuro-ocular syndrome of angiomatosis of the

central nervous system. Clinically, mental defect and epilepsy with a subsequent akineto-hypertonic syndrome of neurosomatic deterioration were the most conspicuous features of the condition, which developed on a background of congenital vascular malformation of the neuro-ectodermal structures, i. e., the skin and nervous system.

Fig. 10 (case 9).—Frontal section, showing hyperplasia of the choroid plexus, and the spongy and cribiform appearance of the basal ganglia. (Courtesy of Dr. Myrtelle M. Canavan.)

Case 10.—*History.*—M. B., a woman, aged 28, was admitted to the Monson State Hospital on March 22, 1930. Her father, aged 65, had suffered from angina pectoris for the past four years. Her mother used to have severe headaches before marriage and also had fainting spells; there were no convulsions; she would merely "go into a dead faint." At the time of examination she was inclined to faint when in a crowd or watching a parade. She had had rheumatic fever three times; in 1929, she had pneumonia and since then had had valvular heart disease. She had had four children and two miscarriages. The first child was prematurely born and lived only a few days. The second was living and well at the age of 31. The patient was the third child. Then she had had two miscarriages at the third month of gestation. The youngest child was 19, and was living and well.

The patient was a full term baby born following a dry labor without instruments; the head was much deformed, and she had paralysis of the left side that was evident from birth as well as a birthmark on the right side of the forehead. She cut her first teeth at 6 months, talked only at 2 years, and did not walk until 4 years of age because of weakness in the left leg. She had chickenpox at 2, mumps at 4, measles at 6 and whooping cough at 10 years of age. At the age of 2 months convulsions were noticed, and she had had them ever since. The convulsions began and predominated on the paralyzed side; however, they became generalized and were usually severe. Following the convulsions, weakness in the left arm and leg increased; she also had a speech difficulty for a while following a convulsion. At the time of admission, she was having about one attack per week. She had always been feebleminded and did not go to school. Her intelligence quotient was 51.

Fig. 11 (case 10).—Vascular nevus in the area of distribution of the ophthalmic division of the right fifth nerve. (See fig. 12.)

Physical Examination.—The blood pressure was 130 systolic and 66 diastolic. The heart and lungs were normal. The patient was well developed, tall and of rather pleasant appearance except that the face was disfigured with a port-wine birthmark over the right side of the forehead, involving the eyebrow, the upper lid and the right side of the bridge of the nose (fig. 11). She had no other skin anomalies elsewhere on the body. The vascular nevus of the face was of a flat nonhyperplastic type; however, some thickening of the skin with an increase of subcutaneous tissue was evident over the right eyebrow, which overhung the upper eyelid. The application of ice on the forehead in the area of the nevus and in the symmetric area of the normal skin produced vasoconstriction pallor which was much more pronounced and more lasting in the normal skin than in the nevoid skin. The application of a glass tube with hot water produced hyperemia in both areas, but in the area of normal skin hyperemia was followed by vasoconstriction pallor, which was not evident in the nevoid area. Also, a white pressure spot, while more conspicuous in the nevoid

area than in the area of normal skin, disappeared almost instantly in the former, while it was more persistent in the latter. There was a telangiectatic condition of the conjunctival vessels of the right eye which was not very marked. There was no evidence of buphthalmos. The pupils were equal and reacted to light and in accommodation. There was no oculomotor paralysis; however, there was some difficulty in turning the eyeballs laterally without associate rotation of the head. The eyegrounds appeared normal. The hemiplegia involving the left side of the face, left arm and leg was not very conspicuous. There was only moderate atrophy of the extremities on the left side. Permanent contracture was entirely absent, but there was a great deal of intention spasm during voluntary movements, the latter bringing out the characteristic hemiplegic attitude of the left arm and hand and the left leg and foot. The voluntary paralysis was not pronounced; it dealt merely with weakness, especially in the left arm. The tendon reflexes were somewhat exaggerated, especially on the left side. The abdominal reflexes were all present and were equal on the two sides. There was a combined flexion sign and Barré sign on the left leg; tonic postural reflexes were abolished in the left ankle. The plantar reflex on the right was of the extensor type; on the left (hemiplegic) side the response was not constant; sometimes good flexion movement of the toes was observed, sometimes jerky extension spasm occurred with retraction of the toe. The great toe on the left foot often showed a spontaneous extension spasm with retraction of the proximal phalanx and flexion of the distal phalanx. This occurred especially under the influence of external stimulation and during effort. There was no evidence of exaggerated spinal reflexes of defense (no flexion withdrawal of the lower extremities). There was no sensory disturbance, except one striking feature; any stimulation, especially sudden and unexpected or painful, applied to any area of the skin on the left side of the body was accompanied by an emotional outburst. The patient stated that she was "very ticklish on her left side." It was noted also that a sudden noise—a reflex hammer dropped on the floor—provoked a generalized twitching in the left arm and leg with an increase of spasm in the left toe and in the left arm. There was no audible bruit on auscultation over the head. A roentgenogram of the skull showed a whirl of calcified blood vessels in the right frontoparietal region (fig. 12).

Comment.—The port-wine nevus involving the area of the right upper division and overlapping slightly the middle division of the trigeminal nerve, together with congenital mental defect, epilepsy from early infancy and the contralateral hemiplegia, presents a full picture of the vascular neurocutaneous syndrome of encephalotrigeminal variety. The roentgenogram of the skull showing a calcified angioma in the right hemisphere gave concrete evidence of the cerebral involvement by the congenital angiomatous malformation. The clinical observations, without an audible bruit, indicate that we deal in this case with the venous variety of angiomatosis, the "angioma venosum" of Cushing and Bailey.

The deficiency of vasomotor innervation in the area of the trigeminal nevus was indicated by the results of simple clinical tests, such as hot and cold applications and of white pressure spots.

The hemiplegia exhibited interesting features; it was not a common infantile hemiplegia; it was characterized more by spasm and intention hypertonia than by paralysis and permanent contracture. There was no evidence of exaggeration of spinal automatism; on the contrary, the midbrain automatism was distinctly exaggerated on the left side, as was shown by the increase of intention hypertonia with automatic emotional and motor reactions induced by stimulation, especially those provided with "thalamic appeal" in the sense of Henry Head. The patient stated that "she is more ticklish on the left side," which indicates an increased sensory thalamic tone on the left half of the body. On general neurologic grounds one may explain the particular syndrome presented by this patient as the result of liberation of subcortical levels, by a widespread congenital lesion of the cortex.

Fig. 12 (case 10).—Roentgenogram, showing a calcified angioma, convoluted in appearance, involving the right hemisphere, ipsolateral with a trigeminal nevus (see fig. 11), and causing contralateral hemiplegia and epilepsy from early infancy.

Case 11.—*History.*—H. C., a man, was admitted to the Monson State Hospital in July, 1911, when aged 10. His mother had had six children and two miscarriages. Three of her children died in infancy or in early childhood. Two were living and well. The patient was the third child. The father was living and well. None of the patient's relatives had birthmarks. The patient was a full term baby; he was born with a port-wine nevus on the left side of the forehead. When 9 months of age, he was taken ill with what the physician called spinal meningitis. The right arm and right leg were paralyzed, and he had an internal squint of the left eye. The paralysis improved, but the squint remained. It is stated that he learned to walk and to talk at the average age. At the age of 2 years, the parents noticed that he was not as intelligent as other children. He acted queerly, was very stubborn and had temper tantrums. After the illness at 9 months, he began to have convulsions; at first rare, they became more frequent and more severe, until at the time of admission to this hospital he had them almost every week.

Course Since Admission.—When 14, the patient was examined by an ophthalmologist who found "double vision O. S. to the left" and a "tumorous mass on the right eyeball at the inner canthus." "This mass was growing and became protruding through the palpebral opening at the inner canthus." The growth "was removed by cutting the pedicle, which was small." Moreover, a double internal rectus tenotomy was performed to correct the strabismus, following which the double vision was much improved.

In the course of the nineteen years during which he had been an inmate of this hospital there was noted a slow but steady increase in the number of convulsions. He developed a tendency to status epilepticus or fits in series, with long free intervals. For the last eight years he was confined to the ward for demented patients, and for the last two or three years he was permanently confined to bed because of generalized muscular rigidity with contractures predominating in the lower extremities and advanced dementia; however, when assisted, he could stand on his feet and take a few steps.

Fig. 13 (case 11).—Vascular nevus in the area of distribution of the first and second divisions of the left trigeminal nerve. Note the hyperplasia of the eyebrows and the fibrous polypi. The patient had had hemiparesis on the right side from infancy.

Apart from the akineto-hypertonic syndrome with bilateral pyramidal and pseudobulbar symptoms which developed in later years, the patient presented Weber's syndrome (hemiplegia alternans abducento-facialis) with deafness in the left ear and probably anesthesia of the left trigeminal area.

The port-wine nevus, as shown in figure 13, was very extensive, involving practically the whole left side of the forehead and scalp, the left upper brow and eye, the left temple and part of the cheek. Over the eyebrow the integument was thickened and cavernous in consistency. Several polypi like those in case 9 were present in the area of the vascular nevus. There were no other skin anomalies except a typical "café au lait" spot about 1 inch (2.5 cm.) long and ½ inch (1.27 cm.) wide on the lower part of the sternum. The left eyeball was distinctly protruding as compared with the right (buphthalmos). The left side of the head and face appeared to be broader, as if hypertrophic. The right pupil reacted to light; the left reacted very sluggishly and was irregular in outline. The left eyeground showed an optic atrophy with a distinct increase of retinal vasculari-

zation. There was no evidence of tumorous masses in the eyeground. The nevoid condition of the retina was evident also by the brilliant red reflection in the left eye when it was illuminated at the proper angle (albino eyes).

Comment.—It is probable that the acute illness at 9 months of age, followed by crossed hemiplegia with involvement of the left abducens and left facial nerves, was caused by a pontile hemorrhage from a cerebral angioma. The onset of the condition was apparently accompanied by acute symptoms and fever, which was diagnosed as spinal meningitis. The rise of temperature in pontile hemorrhages is very common (Leyser, Oppenheim and Kufs), thus easily causing confusion with acute inflammatory processes in the central nervous system.

The previous history, the present neurologic condition, with epilepsy, akineto-hypertonic syndrome and dementia, associated with vascular nevus of trigeminal distribution, indicate an involvement of the central nervous system by a congenital angiomatous malformation. The port-wine nevus had several typical fibrous polypi (fig. 13), apparently identical with those of Recklinghausen's neurofibromatosis. The record indicates that at 14 years of age a pedunculated polyp growing on the right eyeball was removed. Moreover, the patient had a characteristic "café au lait" spot on the chest. These three features of skin anomalies establish almost a complete neurocutaneous syndrome of Recklinghausen's disease, combined with the vascular neurocutaneous syndrome of encephalotrigeminal variety.

Case 12.—*History.*—D. L., a woman, aged 25, was admitted to the Monson State Hospital in June, 1919. Her mother had warts and moles scattered over her body. She had two polypi on the neck, which once were dark brown moles. Several of the patient's brothers and sisters had polypi and brown moles on their skin, which were as large as a pea at birth and when examined were as large as a thumb-nail. One of the patient's brothers had a brown hairy mole on the middle of his back as large as the palm of the hand. This was not present at birth. Another brother at birth had small red marks as large as a thumb-nail and of the same color as those on the patient's face. They were present on the nose, eyelids and lips. They gradually faded out so that when he was about 1 year of age they disappeared. The mother of the patient, aged 61, had had fainting spells since the age of 13, and a few years before this history was taken she had what her daughter called a "real fit." Her teeth were set, and she convulsed, frothed and was unconscious. She had had nine children and one miscarriage. The patient's paternal grandmother died at 72 years of age of what was called locomotor ataxia. For the last few years of life she was blind, and for several years before death she was nervous and in poor health. The patient's father suffered with severe sick headaches for many years and died in a State Hospital for the Insane after he had spent nine years there. His case was diagnosed as involutional melancholia, with arteriosclerosis of the brain. The oldest sister of the patient, aged 37, had suffered with migraine since the age of 10. She was very nervous and occasionally had hallucinations, especially at night. When about 2, she had convulsions and had had fainting spells ever since. One brother, aged 35, suffered from severe headaches, was nervous, and "sometimes

during the night saw hands coming after him." He had had convulsions lasting for twenty-four hours when he was 6. His daughter had convulsions when aged 1 year. The third brother of the patient died in convulsions at 8 months of age. A sister of the patient, aged 23, had had convulsions in infancy. The third sister, aged 22, and a brother, aged 33, were in good health.

The patient was the eighth child, born at full term, without instruments, and appeared to be a normal baby except for a port-wine birthmark on the right side of the forehead, nose and cheek. At 3 years, she had measles. She developed normally and went to school at 6 years. When about 9, she began to have fits and had continued to have them ever since. When 13, she was admitted to the Monson State Hospital.

Examination.—On admission, no neurologic signs were found. There was no paralysis or contractures. The body attitude and gait were normal. The patellar reflexes, however, were exaggerated. Mentally she was much deteriorated.

Course.—With increasing frequency of convulsions, the deterioration continued to progress. At the age of 16, she had on an average thirty fits per month. For a while the frequency of convulsions remained stationary; then slow but steady regression of the number of convulsions took place so that at the age of 21 she had an average of fifteen fits per month; since that time they had decreased gradually to six seizures per month, and in the last nine months (1930) she had an average of three seizures per month. While the epileptic fits were decreasing in frequency, the deterioration, both psychic and physical, became very pronounced. She developed an akineto-hypertonic syndrome with generalized muscular rigidity, flexion attitude of the head, trunk and extremities, bilateral pyramidal symptoms and profound dementia.

Present Condition: There was a flat vascular nevus on the right side of the forehead and a few small ones below it on the cheek, nose and upper lip (fig. 14). Also, she had a pigmented mole on the back over the right shoulder blade, another on the same side over the lower rib, a pigmented flat nevus the size of a nickel on the right side of the abdomen near the umbilicus, a few small, raised, pale, fibroid nevi and a "café au lait" spot on the right shoulder. The right eyeball was slightly larger than the left; the right pupil was larger than the left; both pupils reacted to light and in accommodation. On illumination of the pupils, a brilliant red reflection was seen in the right eye; on examination of the eyegrounds, the retinal vessels of the right eye appeared to be distinctly increased in number and turgescent. The right optic disk was hazy in outline and appeared congested. The left eyeground also showed increased vascularity, but not so pronounced as the right. The left optic disk was flat with clear edges. The voluntary movements were slow and awkward, without evidence of paralysis or contractures; there were myoclonic twitchings of the head and shoulders; the whole body was held rigid, with the trunk inclined forward and the arms flexed at the elbows. The tendon reflexes were exaggerated in both upper and lower extremities, without being asymmetrical. The abdominal reflexes were present on both sides. The plantar reflexes were extensor on both sides.

Comment.—In this case there is an interesting example of a combined heredity transmitted to the patient from both paternal and maternal sides. On the paternal side, a nervous disease of an undetermined nature in the grandmother, migraine and organic dementia in the father and migraine and psychopathic disposition in one sister and a brother were good evidence of the hereditary neuropathic predis-

position that was transmitted to the patient. On the maternal side, congenital ectodermal malformations, that is, abortive neurofibromatosis in the mother and in several brothers and sisters, a vascular nevus in one brother and the convulsive disposition, namely, fainting spells and epileptic fits in the mother, and infantile convulsions in several brothers and sisters, were manifest in the patient as a dominant hereditary trait. She presented an encephalotrigeminal vascular syndrome, combined with evidence of abortive neurofibromatosis and associated with epilepsy and mental defect. On the background of the

Fig. 14 (case 12).—Vascular nevus in the area of distribution of the first part of the second division of the right trigeminal nerve.

congenital ectodermal malformations there developed further neurosomatic deterioration as is often observed in the evolution of the chronic convulsive state.

Case 13.—*History.*—J. C., a boy, aged 9, in whose family history nothing important was found, was the second of three children. He was born at full term with instruments and some injury to the head which was not clearly described. A port-wine mark on the right side of the face was present at birth. At 6 months, he began to have convulsions and had continued to have them ever since. When he was about 8 months, his mother noticed that the left side was paralyzed; lately, the paralysis was becoming more pronounced. He cut teeth at 2 years; he began to talk in the third year of life, and he learned to walk after he was 3. The convulsions became more frequent and severe, usually beginning on the paralyzed side. When 6, he was admitted to the Monson State Hospital.

Present Condition.—The patient had a vascular nevus on the right side of the forehead (fig. 15), from the midline to the right temple, extending downward over the right brow, the upper lid and the right side of the bridge of the nose. There was increased vascularity in the conjunctiva of the right eye, and the inner half of the lower lid was involved by the nevus. There was a left infantile hemiplegia with contractures and hypoplasia of the extremities. The patient was restless, though he had a cheerful disposition and usually met the physician with a shower of incoherent questions. Psychometric tests showed an intelligence quotient of 29. During the last two years, convulsions had become more frequent.

Comment.—The presence of a trigeminal nevus, with contralateral hemiplegia, mental defect and epilepsy suggests that the nevoid condition of the blood vessels is reflected in the brain. In this case there is

Fig. 15 (case 13).—Vascular nevus in the area of the first and second divisions of the right trigeminal nerve. The patient had contralateral hemiplegia.

a typical congenital encephalotrigeminal neurocutaneous syndrome of vascular type. It is possible that the patient had a cerebral hemorrhage from the intracranial angioma induced during instrumental delivery. Convulsions were noticed at 6 months, and paralysis became apparent at 8 months. However, it is likely that the latter occurred at the time of birth, but became manifest only at the time of first attempt at locomotion.

Case 14.—*History.*—C. D., a woman, aged 43, was admitted to the Monson State Hospital on Nov. 7, 1930. There was nothing of importance in the family history. She was born at full term following instrumental delivery. There was a port-wine birthmark on the face. She had had epilepsy since the age of 8 months.

Present Condition.—There was a vascular nevus on the right side of the forehead involving the right brow and the upper lid. A roentgenogram of the head showed a whorl of the calcified blood vessels in the right occipital region. There

was no paralysis. The patient presented the picture of advanced neurosomatic deterioration, with dementia and characteristic akineto-hypertonic syndrome: generalized muscular rigidity, flexion attitude of the head, trunk and extremities, unsteady gait with short steps and monotonous monosyllabic speech.

Summary.—In summarizing the six case records of congenital encephalotrigeminal syndrome of vascular type, one may note that while contralateral hemiplegia is of common occurrence, being found in cases 9, 10, 11 and 13, no evidence of such focal cerebral lesions was present in cases 12 and 14; in all six cases, however, there were mental defect and epilepsy, and in all except cases 10 and 13 a characteristic clinical picture of progressive neurosomatic deterioration developed on the background of congenital defect. All six cases presented constitutional inferiority of the nervous system caused by maldevelopment of the ectoderm as evidenced by the characteristic neurocutaneous syndrome. In case 11 and especially in case 13, there were distinct hereditary traits; in the latter case, a congenital ectodermosis in the form of abortive Recklinghausen's neurofibromatosis with epilepsy was present in the mother and several brothers and sisters, while in the patient the ectodermal malformation manifested itself as a vascular encephalotrigeminal syndrome and abortive Recklinghausen's disease associated with epilepsy and severe mental defect. The congenital ectodermal defect creates the predisposition, a specific constitutional inferiority: mental deficiency, neuropathic constitution and convulsive state. The subsequent organic lesions, such as angiomatous tumors, hemorrhages, atrophy and sclerosis of the nerve tissue, act as factors promoting the exterioration of constitutional inferiority, aggravating the mental defect and precipitating convulsions.

SUMMARY AND CONCLUSIONS

Three types of congenital neurocutaneous syndromes—Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis and angiomatosis of the brain with trigeminal nevi—have been discussed and a series of fourteen case records illustrating the association of these syndromes with mental defect and epilepsy presented. All three syndromes exhibit remarkable parallelism in their clinical and pathologic manifestations. All three conditions are the result of congenital maldevelopment bearing electively on the organs of ectodermal derivation —nervous system, eyeball, retina and skin. The ectodermal origin of developmental anomalies in these conditions is evident from the tendency of congenital lesions to a metameric distribution in the skin and in the nervous system. However, in the case of vascular nevi, the distribution of nevi seems to correspond with areas of sympathetic innervation rather than with true metameres, suggesting thus that this

congenital vascular anomaly may have its origin in some developmental defect of vasomotor innervation. The relationship of these lesions to the process of folding and of differentiation of embryonal sheets and to the primitive neural tubes is suggested by topographic predilection of the clinical and pathologic manifestations of the three neurocutaneous syndromes to the cephalic and caudal ends of the body. The malformations may bear more or less exclusively on the neuro-ectodermal tissues, as is the case in tuberous sclerosis and in the so-called central Recklinghausen's disease, or may be confined to the mesodermal element such as blood vessels, as is the case in angiomatosis of the brain. However, the mesodermal hyperplasia (connective tissue, fibroblasts and blood vessels) is present in the characteristic lesions of all three congenital conditions, developing either as a parallel associated malformation or as a secondary reaction. Such hyperplasia of connective tissues, fibroblasts, causes tumorous growths of the skin and nerve trunks, polypi arising from Schwann's cells of the nerve filaments. These tumors may be called neurofibroblastomas. The pigmented nevi, which are nerve-ending neuromas, as had been shown by Masson, were believed by Recklinghausen to be lymphangiofibromas on account of the hyperplastic reaction on the part of the mesodermal elements in these tumors. In the port-wine vascular nevi, consisting of hemangiectatic overgrowth of blood vessels, mesodermal hyperplasia altogether overshadows the ectodermal malformation, on the background of which the telangiectasia develops.

The three congenital neurocutaneous syndromes overlap each other in their clinical and pathologic manifestations. This overlapping is shown by the association of the cutaneous manifestations of neurofibromatosis with those of tuberous sclerosis (cases 5, 6, 7 and 8) and with those of angiomatosis (cases 9, 11 and 12). Pathologically, this is exemplified by the close histologic analogies exhibited by the cerebral lesions of Recklinghausen's disease (spongioblastosis) and those of tuberous sclerosis (neurospongioblastosis) and by the occurrence of angiomatosis in association with tuberous sclerosis (Greig) and with neurofibromatosis (Gaupp). Often, pathologic differentiation of the primitive gliomatosis or gliosis and of angiomatosis of the central nervous system into entirely separate entities is impossible. The existence of histogenetically mixed forms (angiogliomatosis) has been pointed to by Roussy and Oberling. Recklinghausen's neurofibromatosis and Bourneville's tuberous sclerosis belong to the group of congenital malformations, probably of earlier date in the course of embryogenesis than the encephalotrigeminal angiomatosis. In the former two conditions one deals with a widespread blastomatosis with congenital tumor formation and profound disorder in the histogenesis

of neuro-ectodermal tissues, affecting mainly the peripheral and central glia. With Bourneville's and Recklinghausen's blastomatosis one may mention also Lindau's hemangioblastomatosis. The encephalotrigeminal angiomatosis probably is a congenital condition of later onset in the course of embryogenesis than the former two, as in this vascular neurocutaneous syndrome one deals not with a true hemangioblastomatosis but, as Cushing and Bailey pointed out, with an angiomatous malformation—hemangiectatic hyperplasia—of differentiated blood vessels. However, all transitions between early neoplastic and late hyperplastic malformations are easily conceivable on the ground that the disturbance of embryonal development may set in at any given moment of the latter's complex course. So, for example, the tumors of the retinas and of the visceral organs are more common in the congenital syndromes of earlier type (Recklinghausen, Bourneville and Lindau's diseases), but they may be met with in the congenital syndrome of the latter type (encephalotrigeminal angiomatosis). All three congenital syndromes have their common origin in a malformation of the ectoblast. Both clinically and pathologically, they all may be included in one group under the term of congenital ectodermoses. The three neurocutaneous syndromes arising on a common ground of congenital ectodermal malformation are not identical. They probably differ, as has been pointed out, in the period of embryogenesis at which the disturbance occurs; they differ also in the predominance of one or other of the ectodermal structures involved and, therefore, in their clinical and pathologic manifestations; they differ also in the degree of participation of mesodermal elements; thus, the mesodermal element is most prominent in the vascular neurocutaneous syndrome, with regard to which the term of congenital ectodermosis of vascular type (ectodermosis telangiectodes) seems to be justified.

It is the ectoderm that carries the most highly differentiated functions of the individual. We have considered mental defect and epilepsy associated with three congenital neurocutaneous syndromes as the result of defective integration of the nervous functions caused by malformation of the primitive ectoderm. We have identified this developmental defect of nervous function with that etiologic component of the convulsive state that is called predisposition.

SUBACUTE COMBINED DEGENERATION OF THE CORD

CHANGES FOLLOWING LIVER THERAPY; A HISTOPATHOLOGIC STUDY *

CHARLES DAVISON, M.D.
NEW YORK

TABLE OF CONTENTS

I. Introduction
II. Material Used and Method of Procedure
III. Report of Cases
1. Cases of Subacute Combined Degeneration in which the Patients Did Not Receive Liver Therapy (Table 1)
2. Cases of Subacute Combined Degeneration in which the Patients Received Liver Therapy (Table 2)
IV. Comment
V. Summary and Conclusions

It is recognized that, clinically, liver therapy produces a beneficial effect in pernicious anemia. The effect of this form of treatment on the spinal cord in subacute combined degeneration is a moot question. The purpose of this study is to determine what influence, if any, liver therapy has on the myelin sheaths, axis cylinders and glial tissue in cases of pernicious anemia presenting neurologic signs and symptoms. An attempt will be made to demonstrate that liver therapy does not cause regeneration of the axis cylinders in the spinal cord and that the only change noted was a glial overgrowth of varying intensity.

In thirty-one cases of pernicious anemia complicated by subacute combined degeneration in which the patients were given liver therapy, Minot and Murphy [1] found improvement in such symptoms as weakness, tingling, disturbances in the vibratory sense and coordination, although the reflexes remained unchanged. In a series of fourteen cases of pernicious anemia with neurologic signs and symptoms, Rich-

* Submitted for publication, March 3, 1931.

* From the Neuropathological Laboratory, Montefiore Hospital.

* Presented at a Meeting of the New York Neurological Society, Dec. 2, 1930, and the Society for Experimental Biology and Medicine, March 18, 1931.

1. Minot, G. R., and Murphy, W. P.: Treatment of Pernicious Anemia by a Special Diet, J. A. M. A. **87**:470 (Aug. 14) 1926; A Diet Rich in Liver in the Treatment of Pernicious Anemia, J. A. M. A. **89**:759 (Sept. 3) 1927.

ardson [2] recorded amelioration in these signs and symptoms in eight cases. Ungley and Suzman,[3] reviewing sixty-one cases of pernicious anemia with subacute combined degeneration, in thirty of which the patients were treated with liver, found considerable improvement in the neurologic manifestations in seventeen cases of the treated group. The thirty-one cases not treated with liver showed no such improvement. Needles,[4] in twenty-five cases of subacute combined degeneration, in eleven of which the patients were treated adequately with liver, observed definite objective and subjective improvement in two cases and cessation of the progression of the disease in four cases. There are a number of other reports recording improvement in cases of subacute combined degeneration, but as each of these reports consists of only one or two cases, the references to this literature are omitted.

The underlying pathologic process in subacute combined degeneration consists of Lueckenfeldern (honeycomb appearance), marked destruction of the myelin sheaths and axis cylinders and regressive glial changes. This study is an attempt to demonstrate that such histopathologic changes are inconsistent with the view that the function of the spinal cord can be restored following liver therapy. It was believed that the only way to arrive at the truth was to study carefully the spinal cords in a number of cases of pernicious anemia with neurologic signs and symptoms of subacute combined degeneration in which the patients had been subjected to liver therapy. It must be stated at the outset that of the patients in this series coming to necropsy, only two showed clinical improvement in the neurologic complications.

MATERIAL USED AND METHOD OF PROCEDURE

Material.—Seventeen cases of pernicious anemia with signs and symptoms of posterior column and pyramidal tract involvement coming to autopsy formed the basis of this study. Of these, ten patients had been under observation prior to the institution of the Minot and Murphy method of treatment (table 1); the remaining seven received liver therapy (table 2).

Method.—The spinal cords were sectioned transversely and longitudinally and were stained by the myelin sheath (modified Weil method), sudan IV, Victoria blue, Mallory phosphotungstic, Bielschowsky, hematoxylin-eosin and cresyl violet methods. Special study was made of the myelin sheaths, axis cylinders and glia.

2. Richardson, W.: Pernicious Anemia; the Results of Treatment with Liver or Its Derivatives in Sixty-Seven Cases, New England J. Med. **200**:540, 1929.

3. Ungley, C. C., and Suzman, M. M.: Subacute Combined Degeneration of the Cord: Symptomatology and Effects of Liver Therapy, Brain **52**:271, 1929.

4. Needles, W.: Personal communication. This work was carried out on patients in the neurologic wards of Montefiore Hospital.

TABLE 1.—*Patients with Subacute Combined Degeneration Who Did Not Receive Liver Therapy*

No.	Sex	Age	Duration of Illness	Blood Picture					Gastric Analysis	Clinical Changes		Type of Glial Reaction	Comments
				Hemoglobin	Red Cells	Color Index	White Cells	Differential Stain		Neurologic Signs	in the Spinal Cord		
1	M	46	8 mo.	37	1,632,000	1.13	600	Picture of typical pernicious anemia	Not done	+	+	Regressive	
2	F	48	3 yr.	35	1,370,000	1.28	5,200	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	
3	F	45	2½ yr.	44	1,400,000	1.57	3,200	Picture of typical pernicious anemia	Achlorhydria	+	—	--	This case did not show changes in the spinal cord
4	F	65	2 yr.	40	1,450,000	1.38	5,900	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	
5	F	50	4 yr.	68	2,610,000	1.30	7,300	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	
6	F	34	5 yr.	30	1,112,000	1.34	12,500	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	
7	M	42	5 yr.	48	2,100,000	1.14	7,200	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	
8	M	40	1½ yr.	38	1,500,000	1.27	4,600	Picture of typical pernicious anemia	Not done	+	+	Regressive	
9	M	43	6 yr.	20	920,000	1.56	8,300	Picture of typical pernicious anemia	Not done	+	+	Regressive	
10	M	41	6½ yr.	30	700,000	2.14	7,000	Picture of typical pernicious anemia	Achlorhydria	+	+	Regressive	

TABLE 2.—*Patients with Subacute Combined Degeneration Who Received Liver Therapy*

No.	Sex	Age	Duration of Illness	Blood Picture					Gastric Analysis	Clinical Neurologic Signs	Changes in the Spinal Cord	Liver Therapy		Type of Glial Reaction
				Hemoglobin	Red Cells	Color Index	White Cells	Differential Stain				Length of Period	Improvement Following Liver Therapy	
1	F	65	2 yr., 7 mo.	83	3,840,000	1.09	5,700	Anisocytosis, poikilocytosis	Achlorhydria	14 mo. before death	Subacute combined degeneration	14 mo.	+	Progressive; marked gliosis
2	F	63	6 mo.	69	3,800,000	0.69	5,800	Normal blood picture	Achlorhydria	3½ mo.	Subacute combined degeneration	2 mo.	—	Progressive; marked gliosis
3	F	52	4½ yr.	44	2,040,000	1.10	5,900	Typical pernicious anemia blood picture	Achlorhydria	4½ yr.	Subacute combined degeneration	14 mo.	—	Progressive; marked gliosis
4	F	58	3 yr.	79	3,680,000	1.09	7,000	Normal blood picture	Achlorhydria	3 yr.	Subacute combined degeneration	6 mo.	—	Progressive; moderate gliosis
5	F	55	5 yr.	64	3,280,000	0.98	7,800	Anisocytosis, poikilocytosis, normoblasts	Achlorhydria	5 yr.	Subacute combined degeneration	3 yr.	+	Progressive; moderate gliosis
6	F	54	2½ yr.	74	4,184,000	0.90	3,800	Anisocytosis, poikilocytosis, normoblasts	Achlorhydria	6 mo.	Subacute combined degeneration	2½ yr.	—	Progressive; moderate gliosis
7	M	39	2½ yr.	50	1,900,000	1.31	5,800	Typical blood picture of pernicious anemia	Achlorhydria	18 mo.	Subacute combined degeneration	16 mo.	—	Progressive; moderate gliosis

• This blood count was taken before the institution of liver therapy, and it was never typical of pernicious anemia.

Only those sections were studied in which the changes were found both in the posterior columns and in the pyramidal tracts, and which presented the typical picture seen in subacute combined degeneration, viz., Lueckenfeldern, destruction of myelin sheaths and axis cylinders, and poor glial response. In the sections in which the pyramidal tracts or the posterior columns alone were involved and did not present the Lueckenfeldern, but showed an isomorphous gliosis, the process was considered to be due to a descending or an ascending degeneration. This is important for an understanding of the changes in the spinal cord following liver therapy.

Fig. 1.—Transverse section of the midthoracic region showing demyelination of the posterior and lateral columns. (This patient did not receive liver therapy.) Myelin sheath stain (modified Weil method); × 30.

The material from cases of subacute combined degeneration with no history of liver therapy was studied only for comparative purposes. Changes in the myelin sheaths, axis cylinders and glia in these sections were compared with those from the cases in which the patients had had the benefit of liver therapy.

It will not be necessary to describe the detailed histopathology of subacute combined degeneration. It should be emphasized, however, that the glial reaction in cases of subacute combined degeneration is designated as a regressive glial change.

REPORT OF CASES

CASES OF SUBACUTE COMBINED DEGENERATION IN WHICH THE PATIENTS DID NOT RECEIVE LIVER THERAPY (TABLE 1)

Ten cases form the basis of table 1. For the purpose of this study the detailed histories, physical signs and histopathologic descriptions are deemed unnecessary and are therefore omitted. Photomicrographs from cases of subacute combined degeneration in which the patients received no liver are given for comparison with cases in which the patients were treated with liver. Myelin sheath, Bielschowsky and Victoria blue sections suffice to illustrate the changes induced. These are

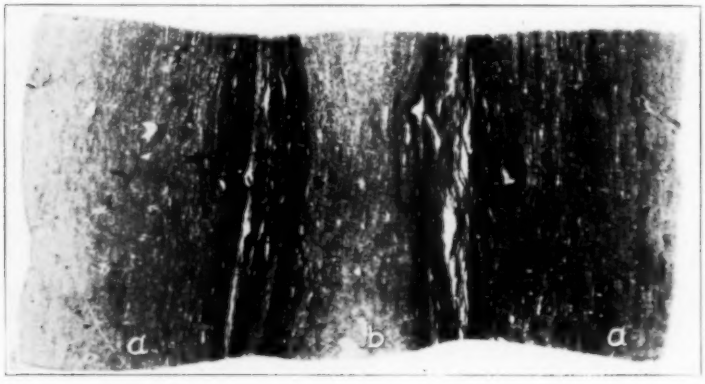

Fig. 2.—Longitudinal section from the upper thoracic cord showing demyelination of (*a*) lateral pyramidal tracts and (*b*) posterior columns. (This patient did not receive liver therapy.) Myelin sheath stain (modified Weil method); × 30.

typical sections from one case in table 1, and illustrate the alterations found in the other cases. In the myelin sheath sections (figs. 1 and 2), the pyramidal tracts and part of the posterior columns are demyelinated. In the Victoria blue preparations, the staining is fairly uniform, and the honeycomb appearance of the cord and the lack of glial productivity can be discerned easily even in the low-power photograph (fig. 3 *A*). With a higher power the common changes observed in the myelin sheath stain (fig. 4) were those of almost complete disintegration. In the Bielschowsky stain (fig. 5) the axis cylinders were broken down; some were swollen and had a corkscrew appearance. With a higher power the poor glial response, or regressive glial changes, the honeycomb appearance, and the complete absence of glial productivity can readily be seen in the Victoria blue preparations (fig. 6 *A*). This is best illustrated when compared with the glia fibers from a normal spinal cord (fig. 6 *B*).

CASES OF SUBACUTE COMBINED DEGENERATION IN WHICH THE PATIENTS RECEIVED LIVER THERAPY (TABLE 2)

This group comprises seven cases that came to autopsy. The outstanding changes observed in the cords, in contrast to those of the preceding group, consisted of a varying degree of gliosis. In some cases this was moderate, in others marked. Detailed histories of the cases will be omitted. For the detailed blood

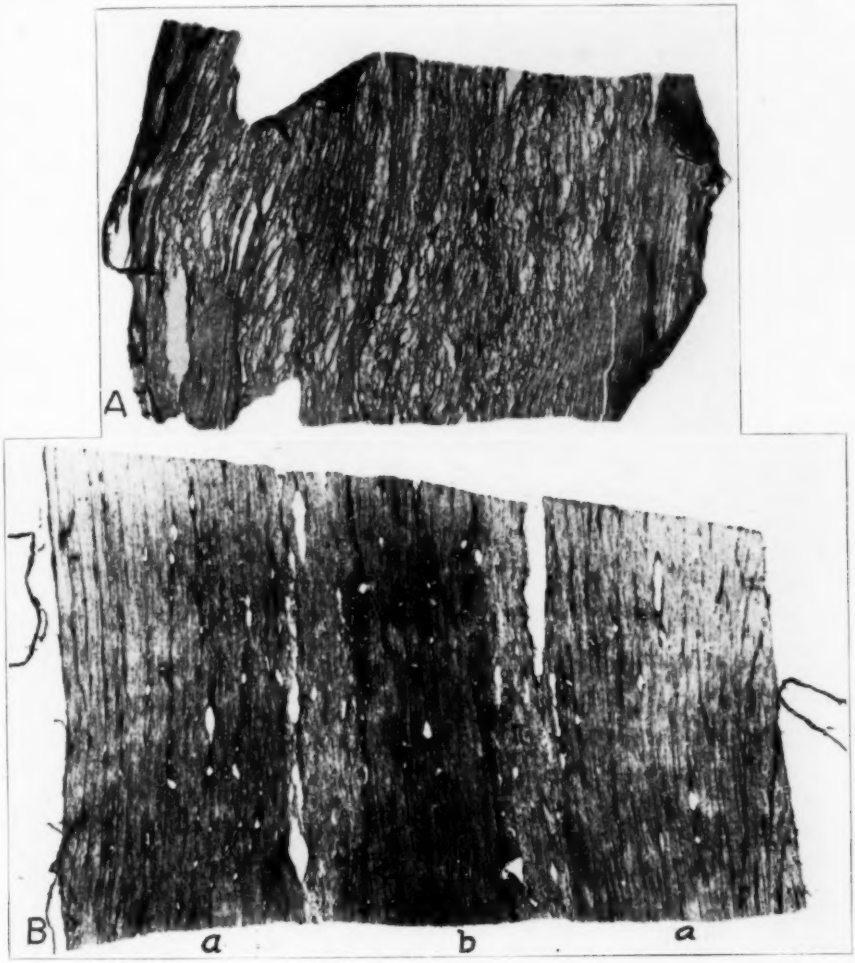

Fig. 3.—*A*, same section as figure 2, showing poor glial response in the demyelinated area. Victoria blue stain; × 30. Compare with *B*, showing normal spinal cord. *B*, longitudinal section from a normal spinal cord showing the normal appearance of the glia in (*a*) lateral pyramidal tracts and (*b*) posterior columns. Victoria blue stains; × 30.

picture and gastric analysis in these cases, the reader is referred to table 2. A detailed histopathologic report in only two cases will be given, one illustrating marked, the other moderate, gliosis. The reports in the other cases will be briefly summarized.

Fig. 4.—Longitudinal section of the posterior columns showing destruction and swelling of the myelin sheaths. (This patient did not receive liver therapy.) Myelin sheath stain (modified Weil method); reduced from a magnification of × 480.

Fig. 5.—Same as figure 4, showing destruction and swelling of the axis cylinders. Modified Bielschowsky stain; reduced from a magnification of × 480.

Fig. 6 *A*.—Same as figure 3 *A*, showing poor glial response and honeycomb appearance. Victoria blue stain; × 480. Compare with figure 6 *B*, showing the glial fibers in a normal spinal cord.

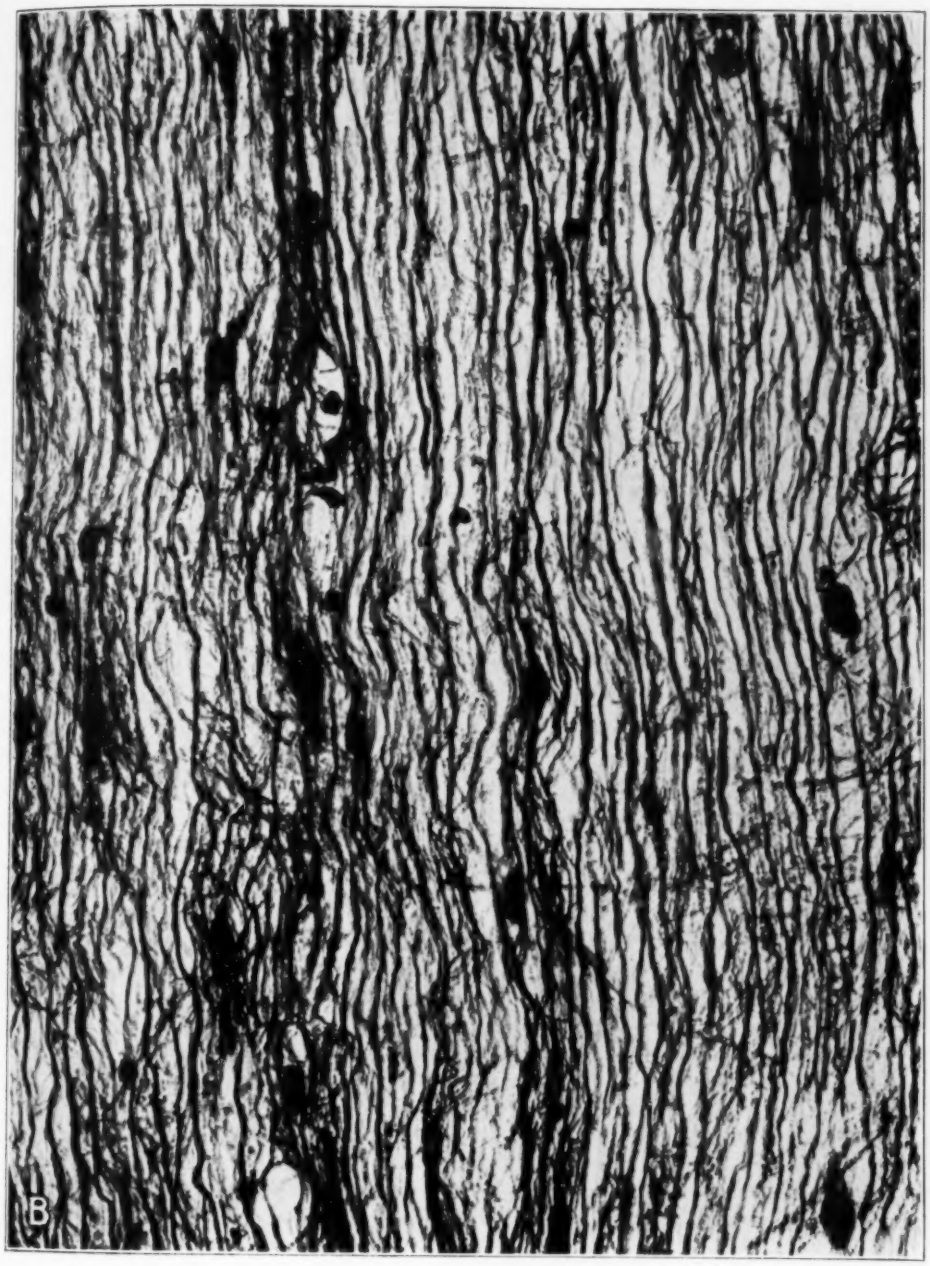

Fig. 6 *B*.—Same as figure 3 *B*, showing the glial fibers from a normal spinal cord. Victoria blue stain; × 480.

CASE 1.—M. M., a woman, aged 65, was admitted to the hospital on Aug. 12, 1929. The pernicious anemia had first appeared in July, 1927. The neurologic symptoms and signs of disease of the posterior columns and pyramidal tracts were first observed in January, 1929, eighteen months after the onset of the disease. Liver therapy was then instituted, and after four weeks of treatment the power of the upper extremities improved considerably, while that of the lower extremities changed but little. The reflexes and sensory conditions, however, remained unchanged. The patient died on March 15, 1930, following several convulsive seizures.

Gross Examination.—The cord was markedly thinned. There was translucency of the posterior columns and crossed pyramidal tracts in all segments.

Microscopic Examination.—Transverse and longitudinal sections at various levels were stained by the methods already indicated.

Fig. 7.—Transverse section of the spinal cord showing demyelination of the posterior and lateral columns. (This patient received liver therapy.) Myelin sheath stain (modified Weil method); × 30.

The spinal cord presented the usual histologic picture seen in subacute combined degeneration. With the myelin sheath stain, the transverse and longitudinal sections showed demyelination of the posterior columns and crossed pyramidal tracts (figs. 7 and 8 *A*). Under a higher power, most of the myelin sheaths in the areas of demyelination were destroyed and the others showed various degrees of swelling and disintegration (fig. 9). With the Bielschowsky method, the axis cylinders of the crossed pyramidal tracts and of the posterior columns had undergone various stages of degeneration, from a fragmentation and corkscrew appearance to a complete destruction (fig. 10). The changes in myelin sheaths and axis cylinders in this case were not different from those in untreated cases of subacute combined degeneration. In the sections stained with the Victoria blue method, however, there was a definite increase in the glia fibers, both in the crossed pyramidal tracts and in the posterior columns (figs. 8 *B*, 11 and 12). It will be noted that the areas of gliosis correspond with the areas in which demyelination was observed

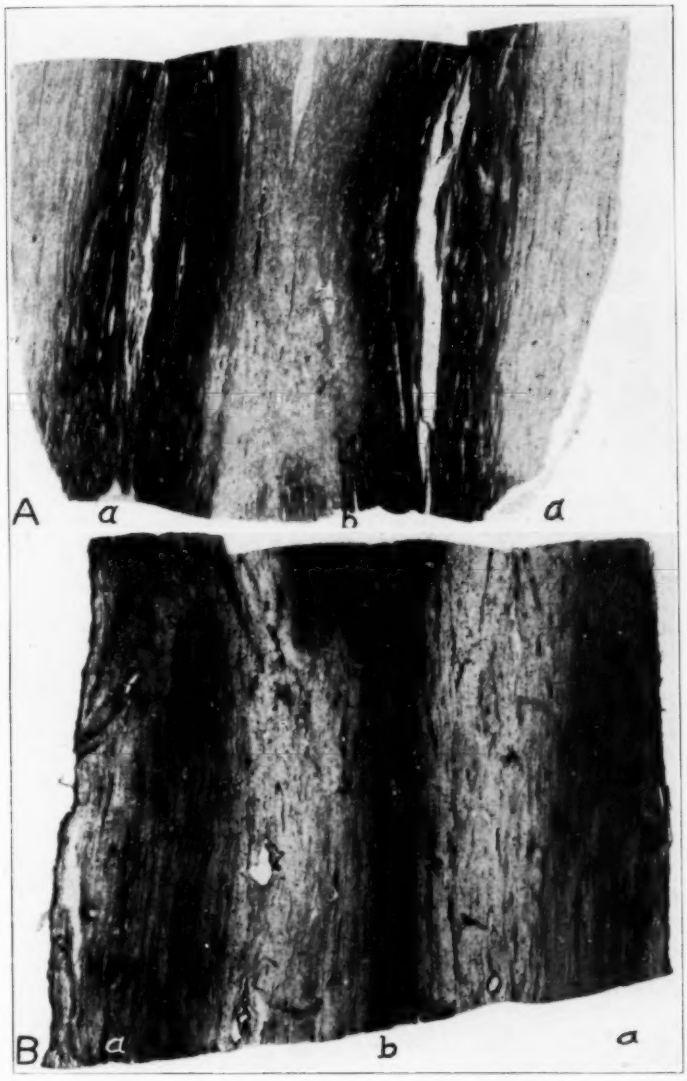

Fig. 8.—*A*, longitudinal section from the upper thoracic cord showing demyelination of (*a*) lateral pyramidal tracts and (*b*) posterior columns. (This patient received liver therapy.) Myelin sheath stain (modified Weil method); × 30. *B*, same as *A*, showing dense gliosis in (*a*) lateral pyramidal tracts and (*b*) posterior columns. Victoria blue stain; × 30. Compare with figs. 3 *A* and *B*.

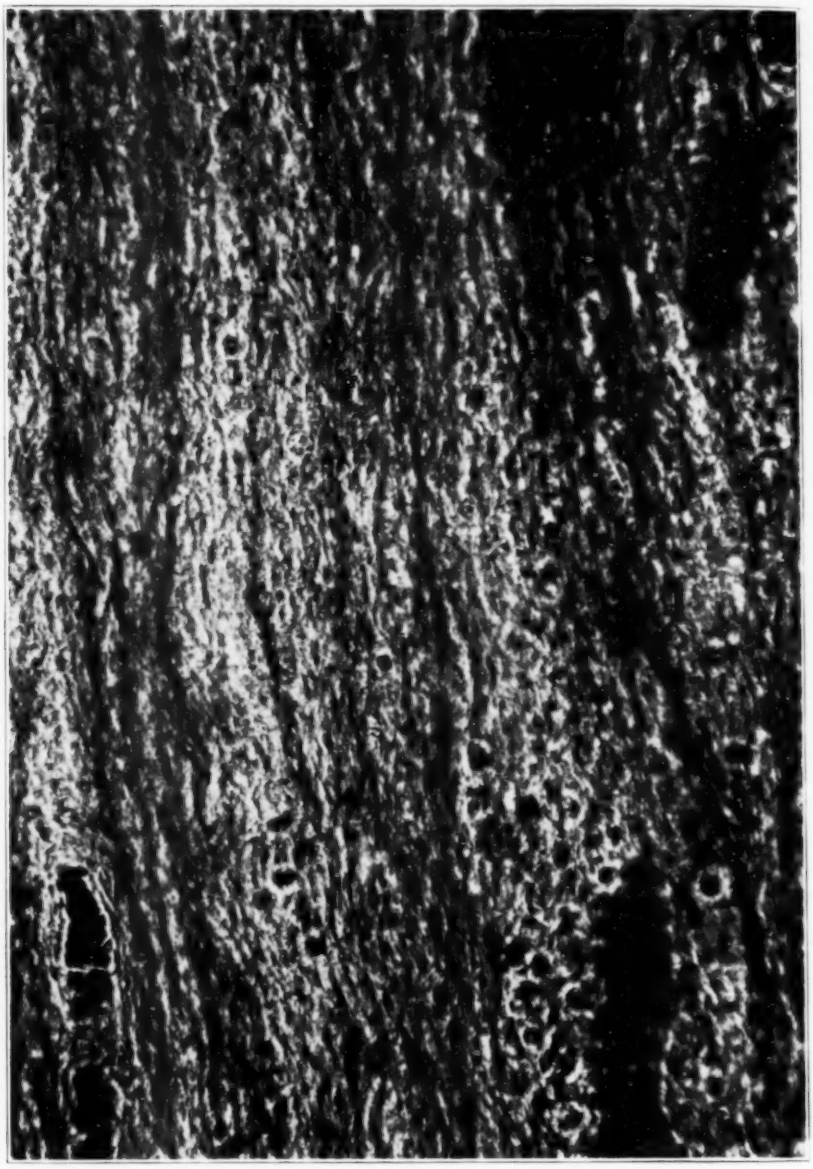

Fig. 9.—Longitudinal section showing destruction of the myelin sheaths. (This patient received liver therapy.) Myelin sheath stain (modified Weil method); reduced from a magnification of × 480.

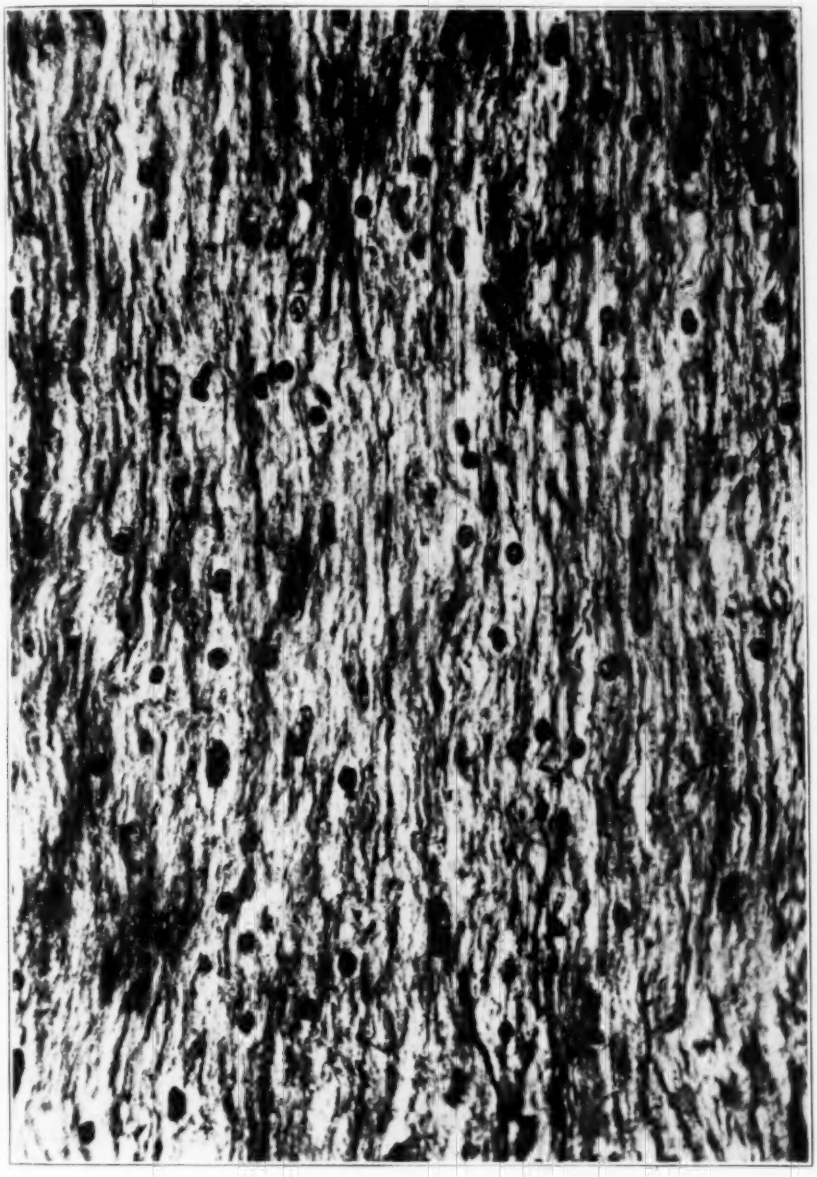

Fig. 10.—Same as figure 9, showing marked destruction of most of the axis cylinders. (This patient received liver therapy.) Modified Bielschowsky stain; reduced from a magnification of × 480.

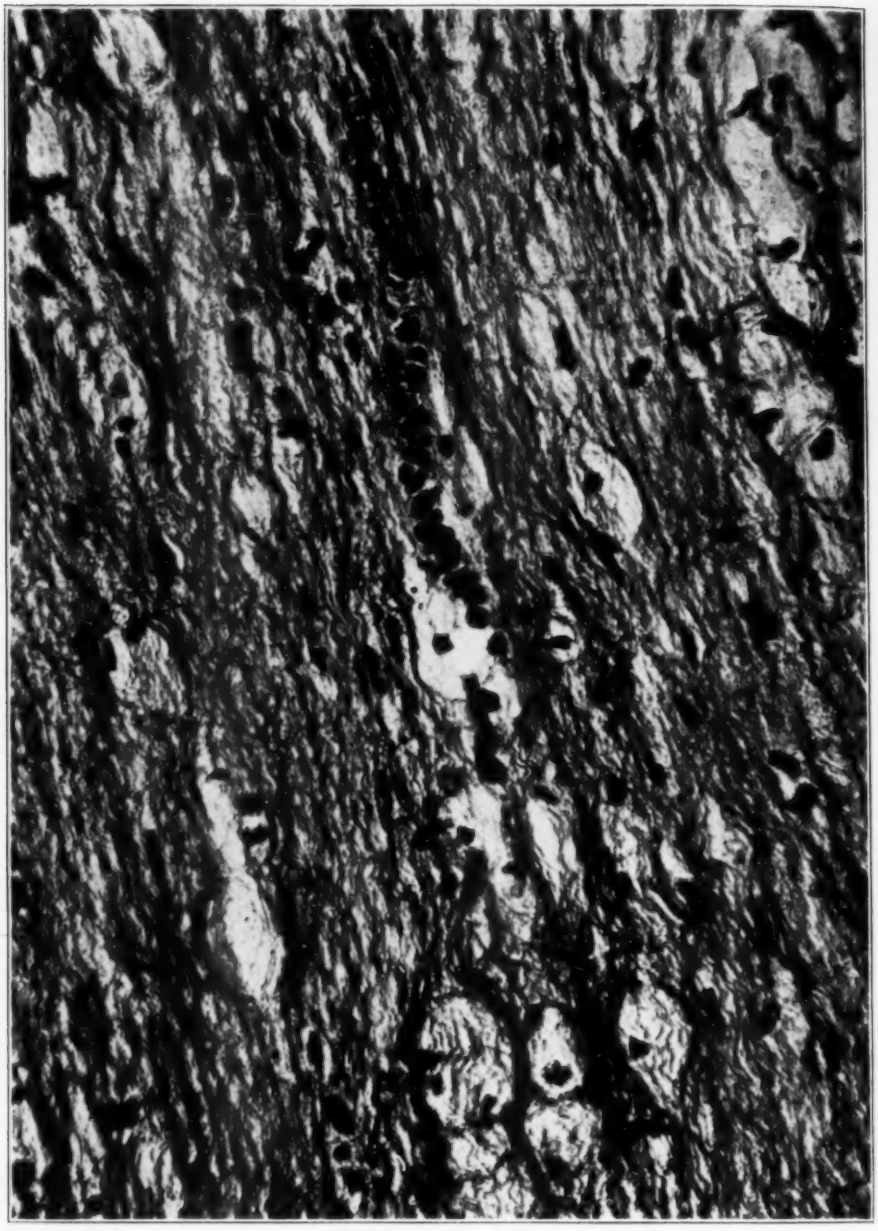

Fig. 11.—Longitudinal section through the crossed pyramidal tracts of the thoracic region showing slight honeycomb appearance and dense gliosis. (This patient received liver therapy.) Victoria blue stain; × 480. Compare with figures 6 *A* and *B*.

Fig. 12.—Longitudinal section showing dense gliosis in the posterior columns. (This patient received liver therapy.) Victoria blue stain; × 480. Compare with figures 6 *A* and *B*.

in sections stained by the myelin sheath method. The areas of glia productivity consisted of closely packed glia fibers running in a parallel direction, and were observed only in the areas of the spinal cord that were demyelinated. The glial productivity could be detected even with the naked eye in stained preparations (fig. 8 *B*). With a higher power, the contrast between the increase in the glia in the sections from the treated cases (figs. 11 and 12), the poor glial response in the untreated cases (fig. 6 *A*) and the status of the glia fibers in the normal spinal cord (fig. 6 *B*) is brought out much better.

Comment.—The glial proliferation of the posterior columns and crossed pyramidal tracts observed in case 1 was not of the type seen in ascending or descending demyelination, i. e., isomorphous gliosis, but consisted of glial productivity, resembling in some respects the progressive glial changes seen in tabes dorsalis, amyotrophic lateral sclerosis and multiple sclerosis. This type of glial proliferation has never been described in subacute combined degeneration. As it occurred also in the other cases in which the patients had been treated, it may be attributed to the liver therapy. This patient had received liver from the onset of the neurologic condition, a period of fourteen months.

CASE 2.—S. L., a woman, aged 63, was admitted to the hospital on Jan. 2, 1930. Pernicious anemia had been diagnosed on Oct. 4, 1929. The neurologic symptoms and signs of disease of the posterior columns and pyramidal tracts were first noticed in January, 1930; the patient was then given liver for a period of two months. Neither the anemia nor the neurologic condition improved. The blood examination never showed a typical picture of pernicious anemia. Gastric analysis revealed achlorhydria. She succumbed to a terminal pneumonia on March 19, 1930.

Gross Examination.—The cord felt soft in the seventh dorsal segment. Throughout the various segments there was translucency of the posterior columns and crossed pyramidal tracts.

Microscopic Examination.—The myelin sheaths, axis cylinders and glia showed the same changes as those described in case 1. The general histopathologic picture was that found in subacute combined degeneration. In addition to the intense glial proliferation in the posterior columns and pyramidal tracts, there were some areas that showed also the typical poor glial response (regressive glial changes) seen in cords from patients with pernicious anemia who had not been treated with liver.

Comment.—This case did not present a blood picture suggestive of pernicious anemia. The patient was subjected to liver therapy for two months before death, without any improvement in the neurologic signs. The glial reaction manifested by the marked productivity in the posterior columns and the crossed pyramidal tracts was due probably to the liver therapy. The gliosis was neither ascending nor descending in type, because it involved the posterior columns as well as the crossed pyramidal tracts in the same section (fig. 8 *B*). The corresponding myelin sheaths and axis cylinders in the areas of glial productivity showed the same changes as those observed in cases of subacute combined degeneration in which treatment with liver had not been administered.

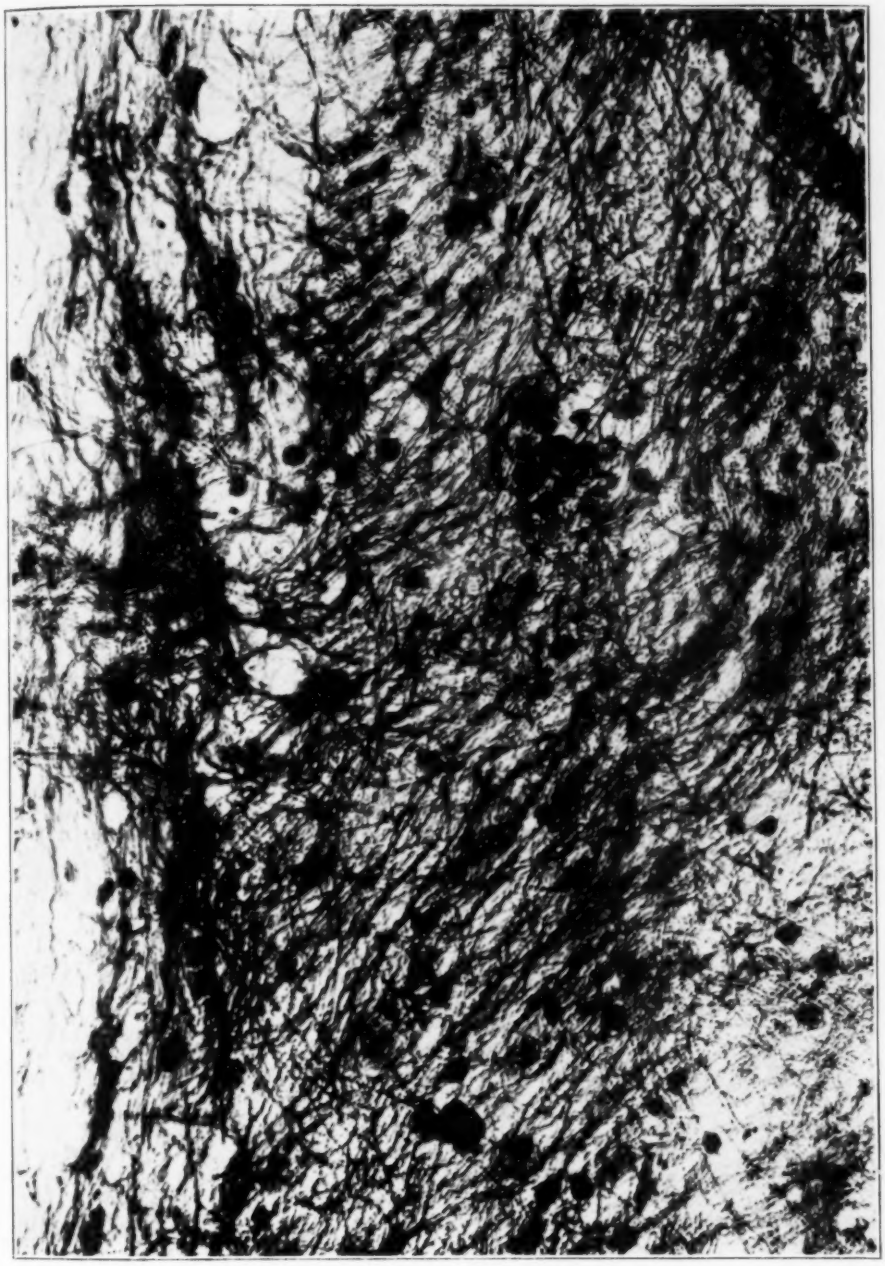

Fig. 13.—Section showing gliosis and criss-cross arrangement of the glia fibers in the lateral pyramidal tracts. (This patient received liver therapy.) Victoria blue stain; × 480. Compare with figures 11 and 6 *A* and *B*.

Case 3.—E. H., a woman, aged 52, was admitted to the hospital on Aug. 20, 1929. Pernicious anemia and subacute combined degeneration had appeared simultaneously in March, 1925. In January, 1929, she was given liver for the first time. A remission occurred, and she remained well for six months. The neurologic signs persisted unchanged. She died on March 20, 1930.

Gross Examination.—On sectioning the cord, translucency of the posterolateral columns was observed.

Microscopic Examination.—The histopathologic picture was the same as in the previous cases. The glia showed definite evidences of productivity in the posterior columns and crossed pyramidal tracts. The changes of the myelin sheaths and axis cylinders were the same as in the untreated cases.

Comment.—This case, in which the patient was under liver therapy for fourteen months, showed no improvement in the neurologic condition. The gliosis, as in the previous cases, was probably due to liver therapy.

Case 4.—F. B., a woman, aged 58, was admitted to the hospital on April 2, 1930. Pernicious anemia and the neurologic signs were first noticed in March, 1927. She received liver from November, 1929, until her death on April 19, 1930, a period of six months. The neurologic condition remained unchanged throughout.

Gross Examination.—There were no abnormalities, except for translucency of the posterolateral columns.

Microscopic Examination.—The myelin sheaths and axis cylinders showed the same changes as those described in the previous cases. With the Victoria blue stain there was observed productivity of the glia in the posterior columns and crossed pyramidal tracts. The gliosis in this and the subsequent three cases differed in two ways from that in the previous three cases. The glia fibers of the crossed pyramidal tracts had a disorderly criss-cross arrangement (fig. 13), rather than a parallel disposition of the fibers. Furthermore, the glial density was less pronounced. The glia fibers of the posterior columns were arranged in a parallel direction (fig. 14).

Comment.—The patient in case 4 did not receive liver until two and a half years after the onset of pernicious anemia and neurologic signs, and remained under this treatment for six months. The gliosis, although less marked than in the previous cases, was easily detected.

Case 5.—A. L., a woman, aged 55, entered the hospital on Aug. 30, 1929. Pernicious anemia and neurologic symptoms and signs were first noticed in 1924. She received four blood transfusions, following which the anemia and neurologic signs pertaining to the posterior columns disappeared. She remained well for two years, when the neurologic signs recurred. On receiving liver and two more transfusions (1926), she again improved for two years (1928) before another relapse occurred. She received liver for three years, until Sept. 4, 1929, when she died.

Gross Examination.—The lower cervical, upper dorsal and middorsal regions showed areas of marked constriction. On cutting the cord at the levels of constriction the various fiber tracts could not be distinguished.

Microscopic Examination.—The histopathologic changes were the same as those in case 4. The gliosis was less intense and the glia fibers of the crossed pyramidal tracts had a criss-cross arrangement.

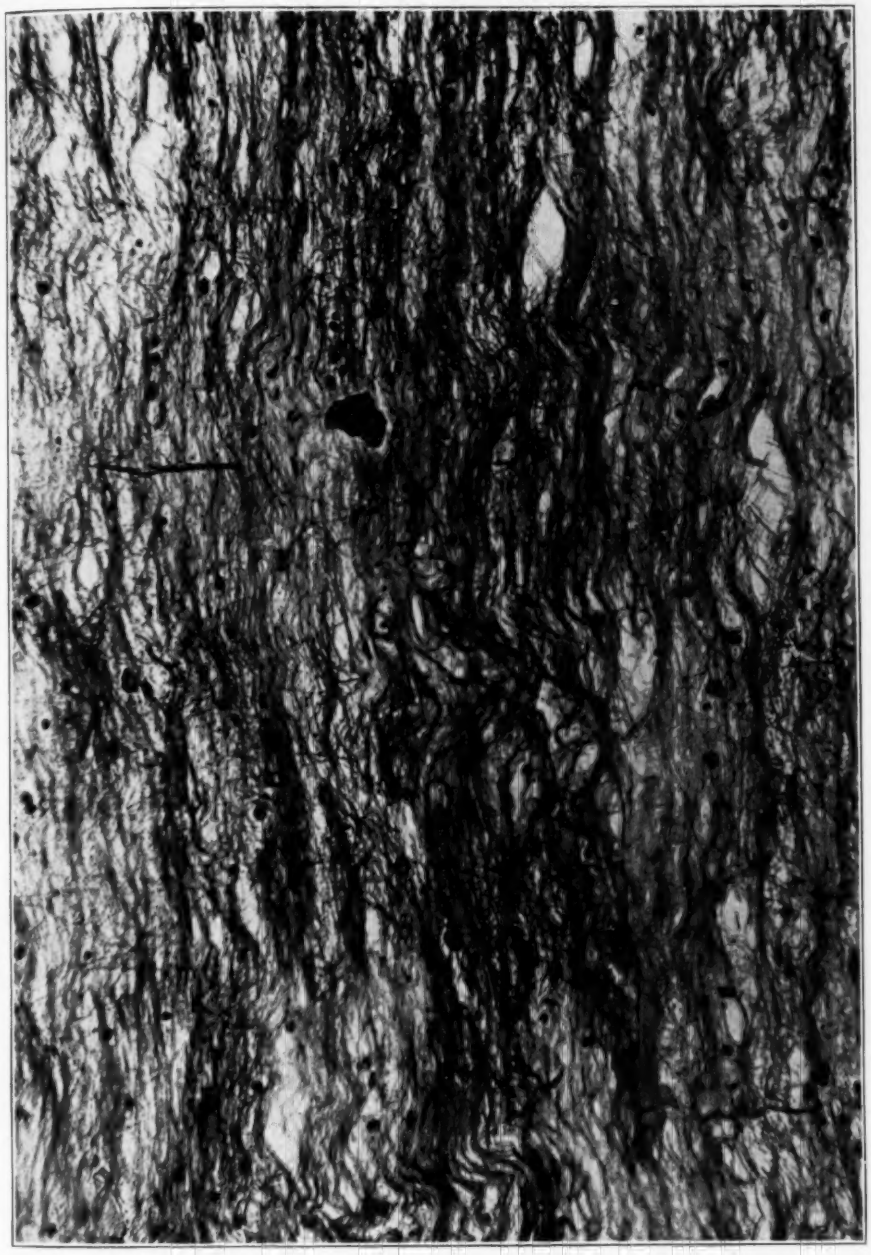

Fig. 14.—Section showing gliosis and parallel arrangement of the glia fibers of the posterior columns. (This patient received liver therapy.) Victoria blue stain; × 480. Compare with figures 6 *A* and *B*.

Comment.—This patient had had two remissions, each lasting about two years, and each following blood transfusions. How much of the proliferative glial response was due to the transfusions and how much to the liver diet I am unprepared to state definitely. In some of the cases in which the patient received transfusions and were not treated with liver (table 1), no such glial changes were observed. I am, therefore, inclined to attribute the progressive glial changes to the liver therapy.

CASE 6.—F. A., a woman, aged 54, was admitted to the hospital on Aug. 21, 1929. Pernicious anemia was first noticed in February, 1927, at which time she was given liver. Following this, she was well for two years. The neurologic signs of disease of the posterior columns and crossed pyramidal tracts were first noticed in May, 1929. The patient was treated with liver for two and one-half years, from the onset of the pernicious anemia until Sept. 1, 1929, when she died of bronchopneumonia.

Gross Examination.—Constrictions of the cord were found in the lower cervical and midthoracic regions. On sectioning the cord in the areas of constriction, all fiber tracts appeared to be destroyed.

Microscopic Examination.—The histopathologic changes were the same as those in cases 4 and 5, except that the glia fibers in this case had a criss-cross arrangement both in the posterior columns and in the crossed pyramidal tracts.

Comment.—It is noteworthy that for two years after receiving liver the patient was sufficiently well to be able to work. The neurologic signs did not appear until six months before death and never changed. The glial productivity was the same as that in the previous cases, except that the fibers had a criss-cross arrangement both in the crossed pyramidal tracts and in the posterior columns.

CASE 7.—I. P., a man, aged 39, was admitted to the hospital on April 21, 1929. Pernicious anemia was first noticed in February, 1927. He received several blood transfusions, with some improvement. In November, 1927, after the transfusions, he showed neurologic signs indicating involvement of the posterior columns. A course of liver therapy was first instituted in January, 1928, and was continued until April, 1929, when he died of bronchopneumonia.

Gross Examination.—There was slight thinning of the cord at the sixth dorsal segment. The posterolateral columns were translucent in all segments.

Microscopic Examination.—The histopathologic picture was the same as that in case 6. The glia fibers of the posterior columns and crossed pyramidal tracts had a criss-cross arrangement.

Comment.—The neurologic signs in this case appeared eighteen months before death, and persisted in spite of the institution of liver therapy sixteen months before death. The spinal cord showed evidences of gliosis of the criss-cross variety as observed in cases 4, 5 and 6.

COMMENT

Clinical Review.—In reviewing the seven cases in which the patients with subacute combined degeneration had received liver therapy, it will be noted that in case 1 the symptoms of pernicious anemia appeared about two and one-half years, and the neurologic signs and symptoms fourteen months, before death. The institution of a liver diet was followed by an improvement of the neurologic signs of the upper extremities. In case 2, the symptoms of pernicious anemia came on six months before death, and the neurologic signs about two and one-half months before death. The patient received a liver diet during the last two months of her illness, without any effect on the neurologic condition. In case 3, the patient evidently had had some neurologic disturbances for four and a half years before a diagnosis of subacute combined degeneration was made. She lived for one year more, receiving liver therapy during that time, with no improvement in the neurologic status. In case 4, the neurologic signs appeared three years before death, but liver was given only in the last six months; no benefit was noted. In case 5, the pernicious anemia and nervous symptoms appeared about five years before death. The patient improved following blood transfusions and was well for two years, when the signs referable to involvement of the posterior columns and pyramidal tracts returned; following two more transfusions and liver therapy there was considerable improvement, which again lasted for two years before the final relapse. Case 6 had presented a picture of pernicious anemia two and one-half years before death. With liver treatment, the patient remained well for two years, when she began to present neurologic signs and symptoms which persisted until death. In case 7, the nervous symptoms were noticed eighteen months before death. Liver therapy administered in the last sixteen months was of no avail.

As can be readily seen from this review, improvement in the neurologic signs and symptoms was observed only in cases 1 and 5. In the latter there is the additional factor of blood transfusions. Liver therapy was not administered early except in case 6; in cases 1, 3, 5, 6 and 7, the patients received liver for one year or more, in cases 2 and 4 for not more than six months. It is difficult to estimate the influence of the liver therapy in delaying the onset of the neurologic signs and symptoms. The administration of liver too late in the disease may account for the lack of improvement in most of these patients.

Histopathologic Observations.—The glial productivity found in patients treated with liver constitutes a progressive glial change and was not observed in untreated patients. In cases 1, 2 and 3, this type of gliosis was a conspicuous feature; in cases 4, 5, 6 and 7 it was less pronounced. The intensity of the glial proliferation does not appear

to depend on the early administration or on the duration of treatment with liver. In cases 4, 5, 6 and 7 the productivity of the glia was designated as disorderly and criss-cross, for the glia fibers did not run in a parallel direction, nor were they as close to each other as those observed in cases 1, 2 and 3 (compare figures). The changes in the myelin sheaths and axis cylinders in the cases of subacute combined degeneration in which the patients were treated with liver were not different from those in the untreated cases. The only change, therefore, that can be ascribed to the liver therapy is the tendency to glial proliferation, a process hitherto unobserved in subacute combined degeneration.

Factors Inducing Improvement in the Neurologic Signs and Symptoms and the Histopathologic Changes in Subacute Combined Degeneration.—When Minot and Murphy [1] noticed improvement in patients with pernicious anemia following liver therapy, they attributed the beneficial results to the improvement in the general condition, coincident with the disappearance of the anemia. Richardson [2] considered the maintenance of the red blood cells at from 4,500,000 to 5,000,00 as the cause of the improvement. Ungley and Suzman [3] contended that "the spinal cord signs of subacute combined degeneration are not the result of the red blood count, as this may occur in the absence of anemia; that the red blood count may be high for long periods on moderate amounts of liver without any improvement in the nervous system; that improvement in the nervous phenomena may commence when the red cell count is as low as 2,000,000 (their case 9); the cessation or diminution of liver may be followed by a relapse of the anemia without any change in the nervous symptoms and signs (their cases 16 and 24)." They consider that "the beneficial effect of liver on the nervous system is a specific phenomenon." One may go a step further and maintain that the beneficial effects of liver in the improvement of the neurologic manifestations, if this contention is accepted, are due to a destruction or diminution of the hypothetical toxin that attacks the myelin sheaths and axis cylinders and induces the regressive glial reaction. Lotmar [5] has produced regressive glia changes in the spinal cord experimentally by injecting the toxins from Bacillus dysenteriae. When the same toxin was administered in smaller quantities or in an attenuated form the glial changes, instead of being regressive, became progressive and resulted in a proliferation of the glia fibers. The histopathologic picture of glial productivity I have found in the seven cases in which the patients were treated by liver

5. Lotmar, F.: Beiträge zur Histologie der acuten Myelitis und Encephalitis sowie verwandter Prozesse, in Nissl and Alzheimer: Histologische und histopathologische Arbeiten ueber die Grosshirnrinde, 1913, vol. 6, p. 245.

favors Lotmar's conception. It may be assumed that in these cases the liver therapy caused a reduction either in the amount or in the strength of the hypothetical toxin, and therefore allowed the glia to proliferate and replace the destroyed tissue. The only possible effect that liver therapy may have on the myelin sheaths and axis cylinders is to arrest the further destruction of these structures. In the light of present knowledge of neurohistopathology, regeneration of destroyed axis cylinders is inconceivable. This explains why the changes in the myelin sheaths and axis cylinders in the seven treated cases were not different from those in the untreated cases. This observation, however, should not discourage one in the early administration of liver in cases of pernicious anemia, with or without neurologic complications. By this procedure, all that may be expected is temporary relief or prolongation of life. To delay the progress of destruction of the axis cylinders and to cause the formation of a glia scar is in itself an advantage.

SUMMARY AND CONCLUSIONS

(*a*) Seventeen cases of pernicious anemia complicated by subacute combined degeneration were studied histopathologically. Seven of the patients had been subjected to liver therapy.

(*b*) Clinically, there was apparent improvement in the neurologic signs and symptoms in only two of the treated patients.

(*c*) Histopathologically, all the treated patients [6] showed progressive glial changes (gliosis). These changes were not observed in the untreated patients with subacute combined degeneration. The myelin sheaths and axis cylinders were not influenced by the liver therapy.

---

6. After this study was completed, two additional cases of subacute combined degeneration in which treatment with liver had been given came to autopsy. These showed the same histopathologic changes as the other seven, namely, gliosis. There had been no improvement in the neurologic signs and symptoms following liver therapy.

IODOBISMITOL IN THE TREATMENT FOR NEUROSYPHILIS *

H. G. MEHRTENS, M.D.
AND
P. S. POUPPIRT, M.D.
SAN FRANCISCO

The popularity of bismuth in the treatment for syphilis has tended to produce a host of preparations. Any new bismuth product should act according to some new principles in order to justify its existence. Most of the products available to the clinician contain the bismuth as cation or in basic form. It has been our experience that these commonly used bismuth preparations seldom penetrate the meninges. In order to secure greater permeability, a bismuth in anionic form seemed preferable, as anions penetrate into the spinal fluid more rapidly than cations. Of the anionic bismuth compounds known on their theoretical side only, sodium iodobismuthite was chosen. Six per cent of this compound was dissolved in ethylene glycol containing 12 per cent of sodium iodide. The name iodobismitol, indicating in abbreviated form the chemical composition and the solvent, was adopted for the product.

PROPERTIES OF THE COMPOUND

Sodium iodobismuthite has the chemical formular $Na_2BiI_5 4H_2O$. The bismuth exists in anionic form, as a complex ion of bismuth and iodine (BiI_5). Iodobismitol injected in doses of 2 cc. contains 0.12 Gm. of sodium iodobismuthite (equal to about 0.026 Gm. of bismuth, or 21.9 per cent). When injected intramuscularly we found very little or no precipitate in the muscles, as indicated by direct inspection of the tissues in animals and by roentgen examinations of patients. Further details on the properties, etc., are given in a separate report.[1]

Local irritation is comparatively mild from a single intramuscular dose of 2 cc. Mehrtens, on taking an injection, felt a stinging sensation for five minutes, a slight discomfort for twelve minutes, no abnormal sensation in an hour and no effects thereafter. In 7,000 injections

* Submitted for publication, June 12, 1930.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

* From the Neuropsychiatric Division, Stanford University Medical School.

1. Hanzlik, P. J.; Mehrtens, H. C.; Girchot, C., and Johnson, C. C.: Iodobismitol, J. A. M. A., to be published.

in 200 patients a great variation of comment on subjective reactions was noted. Most patients complained of some degree of burning, but made little complaint of pain. Some complained of discomfort for an hour. We had no patients who discontinued treatment because of pain, although some had to be encouraged for the first half dozen injections. Induration of tissue was rare when the injection was made deep into the muscle. Improper injections under the skin resulted in induration in from one to three days. No abscesses occurred. The small degree of temporary irritation that occurs immediately after the injection is due mainly to the hypertonicity of the ethylene glycol. Injections of this solvent alone gave about the usual local reaction. Ethylene glycol has the advantage over oil in being soluble in tissue and water, and therefore completely absorbable. In it bismuth compounds are less readily hydrolyzed than in water. It is antiseptic, and its toxicity is low.[2]

TOXICITY

Using the routine rate of injection, i. e., from two to three times per week for months without intermission, there was no evidence of toxicity. Occasionally a bismuth line would appear on the gums, which in the majority of instances we learned to disregard. In no patient with previously normal kidney tests did signs of kidney irritation develop, as judged by urinalysis, or by phenolsulphonpthalein or concentration tests. One case exhibiting badly damaged kidneys before treatment, which prohibited all other antisyphilitic medication, did show decreased kidney functional efficiency after an attempt to use iodobismitol. On the other hand, we had several cases of badly damaged kidneys, which had reacted badly to other forms of antisyphilitic medication, that tended to clear up under treatment with iodobismitol.

Using an intensive schedule of injections, that is, daily injections of 2 cc. for a period of fourteen days, some patients developed a definite bismuth line, but only rarely remarked on a feeling of lethargy. The latter symptom gave us the indication to drop back to an injection interval of twice a week. Even on intensive treatment no demonstrable urinary disturbance appeared. Accidental injection of iodobismitol into the circulation is not to be feared, as intravenous injections, while not recommended, have been given with no untoward effects. We have had six cases exhibiting an iodide rash which disappeared on diminishing the frequency of the injections.

The penetration of this product into the brain and spinal fluid was one of the chief objects of its production. While it is in no way proved that ease of entry into the central nervous system paralleled its

2. Hanzlik; Seidenfeld, and Johnson: J. Pharmacol. & Exper. Therap., in press.

therapeutic effectiveness, we thought that this point was deserving of intensive study. Of forty-one guinea-pigs receiving iodobismitol in repeated therapeutic doses, 92.7 per cent showed bismuth in the brain. Of two moribund patients receiving injections of this product, both showed bismuth in the brain. Of forty patients treated with iodobismitol, 92 per cent showed bismuth in the spinal fluid. These results seemed to indicate that bismuth in anionic form readily penetrates into the central nervous system.

The antisyphilitic action of the product in experimental syphilis of rabbits and on the primary and secondary lesions in man (Alderson) has been shown to be as effective as would be expected from a readily absorbable bismuth, a prophylactic action being more readily produced than a curative action in experimental syphilis.[3]

Clinical and Serologic Results Following Treatment with Iodobismitol in One Hundred Cases of Neurosyphilis

	Meningovascular (32)	Tabes (46)	Dementia Paralytica (22)
Changes in spinal fluid:			
Entirely cleared	7 (21.8%)	.. ..	.. ..
Improved	13 (40.6%)	18 (39%)	11 (50%)
Unimproved	12 (37.5%)	28 (61%)	11 (50%)
Wassermann reaction of blood:			
Entirely cleared	11 (34.3%)	3 (6.5%)	1 (4.5%)
Improved	6 (18.7%)	12 (26.0%)	7 (31.8%)
Unimproved	15 (47.0%)	31 (67.4%)	14 (63.6%)
Clinical changes:			
Improved	25 (78.1%)	26 (56.5%)	13 (59.0%)
Unimproved	7 (21.8%)	20 (43.4%)	9 (40.9%)

Our material consists of 100 neurosyphilitic cases in which iodobismitol was given, the average treatment lasting a year. Many of these cases were tabes of long standing, frequently resistant to other forms of treatment. We realized that these old, far advanced cases included in the series tended to prevent any spectacular result from our present test, but if any favorable results should occur, we could feel confident that the iodobismitol has proved of some definite value. At a later date we hope to report a series of earlier and untreated cases.

The mode of treatment consisted of a deep intramuscular injection of 2 cc. of iodobismitol two or three times a week for at least three months, and in individual cases for six months. Intensive treatment with injections daily or every other day were used only when there seemed to be special clinical indications. Rest periods were not found necessary in the majority of cases. On the contrary, most patients seemed

3. Johnson; Hanzlik; Marshall, and Mehrtens: J. Pharmacol. & Exper. Therap., in press.

to do best when the treatment was uninterrupted. The interval between injections was varied to suit the needs of the individual patient.

One hundred patients were treated for a period averaging a year. Of these cases, thirty-two were meningovascular in type, forty-six were tabes and twenty-two were dementia paralytica. This classification may not be entirely accurate, as several of the patients grouped under the heading of dementia paralytica may properly have belonged in the meningovascular group (see table).

The meningovascular group of thirty-two patients showed 21.8 per cent complete serologic recoveries and 78.1 per cent clinical improvement. This group showed the best results of any of the three groups. It was in this group also that the objective improvements, such as cranial nerve palsies, were evident. That there were unimproved patients to the number of 21.8 per cent in this group is at first surprising, but it must be taken into consideration that there were included some very long-standing cases, accompanied by arteriosclerosis and hypertension.

The tabetic group of forty-six cases showed a serologic improvement in 39 per cent, but no spinal fluids became entirely clear; 56.5 per cent of the patients stated that they were subjectively improved, but in this group we had less objective evidence. The subjective improvements included less than 25 per cent amelioration in root pains. The bladder symptoms were helped, but complete restoration occurred in no case. Difficulties in walking were markedly improved, in spite of the fact that no change in the organic neurologic status occurred. The body weight was frequently increased, and a feeling of well-being was noted in over one half of the cases. Optic atrophy was never improved. It was in this group particularly that difficulty in evaluating the importance of subjective improvement was demonstrated. Only too frequently the enthusiasm of the attendants, and even the thought of receiving a new mode of therapy, tends to produce a temporary feeling of buoyancy in the patient. In this series we tried to discount these factors and to include only such subjective factors in the improvement as continued for many months and seemed to lack any emotional element.

The group of twenty-two cases of dementia paralytica, as already stated, may have contained some cases that would be better classified as meningovascular. This possibly explains why 50 per cent showed improvement serologically and 59 per cent clinically. No case showed a complete return to a normal serology. Twenty-seven per cent of the patients went back to work; the remaining 32 per cent were reported by their families as improved, and seemed to be distinctly better on their visits to the clinic.

The Wassermann reaction of the blood was entirely negative in 34.3 per cent of the meningovascular cases, in 6.5 per cent of the cases of tabes, and 4.5 per cent of those of dementia paralytica. It is interesting that the best results of the treatment in the blood, as well as in the spinal fluid, were obtained in the early cases. These facts suggest that the greatest sphere of usefulness for iodobismitol may ultimately develop in the direction of the field of prophylaxis. The ability of the drug to penetrate the meninges at the time of the primary or secondary manifestations of the disease may tend to avert the later development of neurosyphilis.

An attempt was made to compare the series of cases treated with iodobismitol with a control group treated with other forms of bismuth. This we were unable to accomplish, because all of the available patients were needed to make this series large enough to be of some significance, and also because in the past we had never used bismuth as the sole remedy in neurosyphilis. We were convinced then, and we still believe, that no matter how efficient any antisyphilitic medication may be, that the optimum clinical effect will be secured by a combination of several modes of therapy (including hyperpyrexia) best suited to the individual case.

CONCLUSION

1. Iodobismitol is a soluble bismuth product in anionic form capable of penetrating into the brain and spinal fluid in the great majority of patients.

2. Because of its solubility and freedom from any considerable precipitation in the tissues, it permits great flexibility in varying the medication to the needs of the indivdual case.

3. About 50 per cent of the patients treated for one year were definitely improved clinically and serologically, although many in the series were in an advanced stage and had proved intractable to other forms of antisyphilitic medication. The earlier the treatment was initiated, the more satisfactory was the result.

4. The ability of iodobismitol to penetrate the meninges, when employed during the first stages of the infection, may make it useful in preventing the subsequent development of neurosyphilis.

ABSTRACT OF DISCUSSION

DR. WALTER F. SCHALLER: Because of the available excellent bismuth preparations a new bismuth compound should have obvious and special merit for scientific consideration. The idea that bismuth in an anionic form, represented in this instance by iodobismitol, renders it more permeable and mobile is, so far as I know, a new one. This idea is based on the biochemical fact that the colloidal system of tissues, cells and membranes is negatively charged; we might expect,

therefore, that cationic preparations would be fixed in these structures, whereas the anionic form would be mobile. The therapeutic worth, therefore, of this remedy is theoretically dependent on this mobility. Whereas the circulation of the cerebrospinal fluid may be of considerable importance in the pharmacologic action of iodobismitol, and may depend on its directional flow or lack of flow, the important matter for discussion is the value of mobility and permeability into the central nervous system, and the future of this preparation will largely depend on this particular action.

My personal experience has been rather small, as I have used the drug for eight months and given approximately 200 injections. Since I have used it in association with other antisyphilitic remedies I cannot speak of its absolute value. It is a fine preparation, not painful or toxic, and the subjective improvements have been marked — in this respect similar to the action of tryparsamide. The serologic improvements have been less marked. It will take time, of course, for the preparation to be properly evaluated. It will soon be available for general use.

THE EFFECT OF REMOVAL OF THE STELLATE GANGLIA ON WORMWOOD OIL CONVULSIONS IN CATS*

PETER COHEN, B.S.
AND
LOUIS SPEKTER, B.S.
ROCHESTER, N. Y.

The observation that the exposed brains of epileptic patients under operation have been seen to blanch just before the onset of a convulsion and the recent establishment of the vasomotor control of the cerebral blood vessels have stimulated the investigation of angiospasm as related to the epileptic fit.

Kennedy [1] observed blanching of the parietal cortex before the onset of an attack in a human subject. Foerster [2] described a sequence of events repeatedly seen by him, in epileptic patients, at the operating table: first, the brain becomes pale and sinks away from the skull; then it is suffused with blood and bulges greatly as the convulsion starts.

That the cerebral vessels are under nervous control is generally accepted today, although for many years it was thought that vasomotor nerves were absent in the pial vessels and that the cerebral circulation passively followed the general arterial and venous pressures. The latter point of view seems to have had its origin in the work of Bayliss and Hill [3] and of Hill.[4] Gulland,[5] who did the histologic work, retracted his statement that there were no nerve fibers in the walls of the pial or intracerebral vessels, having found that such nerve fibers exist.

---

* Submitted for publication, May 15, 1931.

* From the Department of Anatomy, the University of Rochester School of Medicine and Dentistry.

1. Kennedy, F.: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567 (May) 1923.

2. Foerster, O.: Die Pathogenese des epileptischen Krampfanfalles: Einleitender Ueberblick, Klinik und Therapie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **44**:746 (Sept.) 1926.

3. Bayliss, W. M., and Hill, L.: On Intracranial Pressure and the Cerebral Circulation, J. Physiol. **18**:324, 1895.

4. Hill, L.: The Physiology and Pathology of Cerebral Circulation, London, J. & A. Churchill, 1896.

5. Gulland, G. L.: Note on Nerve-Fibres to Intracranial Blood Vessels, Rep. Lab. Roy. Coll. Physicians, Edinburgh **6**:55, 1897.

Since then, indirect evidence gathered by Weber,[6] Wiggers[7] and Müller and Siebeck[8] has contradicted the results obtained by Bayliss and Hill. More recently, Forbes and Wolff[9] have presented convincing evidence for the presence of at least a partial vasomotor control of the cerebral blood vessels in mammals. This evidence was obtained from direct observation of the pial vessels in the cat while the cervical sympathetic and vagi were being stimulated. Talbott, Wolff and Cobb[10] demonstrated an increase in the capillary bed of the homolateral cerebral hemisphere after cutting one cervical sympathetic cord. Stöhr,[11] Clark[12] and Hassin[13] have presented further histologic evidence of the presence of nerve fibers in the pial vessels.

Spielmeyer[14] reported changes observed in the cornu ammonis and in the cerebellum of epileptic patients which resemble the changes found in true organic obstruction of the circulation. He expressed the belief that vasomotor disturbances are effective in the mechanism of the epileptic attack.

Cervical sympathectomy has been performed on epileptic patients, but the results reported have not, on the whole, been very encouraging. Winter[15] reviewed the literature on this phase of the subject up to 1902. Lennox and Cobb[16] suggested that sympathectomy should be confined

---

6. Weber, E.: Ueber die Selbständigkeit des Gehirns in der Regulierung seiner Blutversorgung, Arch. f. Physiol., 1908, p. 457.

7. Wiggers, C. J.: On the Action of Adrenalin on the Cerebral Vessels, Am. J. Physiol. **14**:452 (Nov.) 1905.

8. Müller, O., and Siebeck, R.: Ueber die Vasomotoren des Gehirns: Untersuchungen an Tier und Mensch, Ztschr. f. exper. Path. u. Therap. **4**:57 (March) 1907.

9. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

10. Talbott, J. H.; Wolff, H. G., and Cobb, S.: The Cerebral Circulation: VII. Changes in Cerebral Capillary Bed Following Cervical Sympathectomy, Arch. Neurol. & Psychiat. **21**:1102 (May) 1929.

11. Stöhr, P.: Ueber die Innervation der Pia mater und der Plexus chorioideus des Menschen, Ztschr. f. Anat. u. Entwcklngs. Geschichte **63**:562, 1922.

12. Clark, S. L.: Nerve Endings in the Choroid Plexus of the Fourth Ventricle, J. Comp. Neurol. **47**:1 (Dec. 15) 1928.

13. Hassin, G. B.: The Nerve Supply of the Cerebral Blood Vessels: A Histologic Study, Arch. Neurol. & Psychiat. **22**:373 (Aug.) 1929.

14. Spielmeyer, W.: The Anatomic Substratum of the Convulsive State, Arch. Neurol. & Psychiat. **23**:869 (May) 1930.

15. Winter, G. J.: Beiträge zur operativen Behandlung der Epilepsie: Totale und beiderseitige Resection des Halssympatheticus bei der essentiellen Epilepsie nebst 9 eigenen Fällen, Arch. f. klin. Chir. **67**:816, 1902.

16. Lennox, W. G., and Cobb, S.: Epilepsy, Baltimore, Williams & Wilkins Company, 1928.

to patients who exhibit abnormal function of the cervical sympathetic system.

Periarterial sympathectomy has also been practiced as a means of interrupting the path of the sympathetic nerve fibers to the cerebral blood vessels. Some slight degree of improvement has been noted in epileptic patients (Bojovitch,[17] Tinel,[18] Hirsch, Weiss, Izgur and Lauerman [19] and Laignel-Lavastine and Largeau [20]).

Convulsions have been produced in epileptic and in nonepileptic patients by compression of the carotids (Kussmaul and Tenner,[21] Flesch [22] and Tsiminakis [23]). Meagher and Ingraham [24] and Loewy [25] failed to produce seizures by similar methods.

Whether the vasomotor phenomenon is the cause of the epileptic convulsion, or whether it is one of the effects of the "discharging lesion" is of importance in this discussion. This question has recently been discussed by Wilson;[26] he expressed the belief that any vascular factor involved is of neural origin; that is, that the vasomotor center may also come into the path of the discharge.

In order to study epilepsy experimentally, epileptiform convulsions have been induced in animals by the use of convulsant agents. Wormwood oil or absinth has been widely used for that purpose. D'Ormea,[27] from results obtained in an indirect manner, found that there was active

17. Bojovitch, V.: Sympathectomie péri-carotidienne dans le traitement de l'épilepsie essentielle, Rev. de chir. **63**:608, 1925.

18. Tinel, M. J.: Résultats de la sympathectomie périartérielle de la carotide interne dans un cas d'épilepsie essentielle, Rev. neurol. **31**:613 (Nov.) 1925.

19. Hirsch, H. L.; Weiss, M.; Izgur, L., and Lauerman, A.: Periarterial Sympathectomy in Epilepsy, J. A. M. A. **80**:516 (Aug. 13) 1927.

20. Laignel-Lavastine, G., and Largeau, R.: La sympathectomie péri-carotidienne (péri-carotide interne) dans l'épilepsie, Rev. neurol. **1**:1085 (June) 1929.

21. Kussmaul, A., and Tenner, A.: Epileptiform Convulsions Caused by Profuse Bleeding and Also True Epilepsy, translated by E. Bronner, London, New Sydenham Society, 1859.

22. Flesch, J.: Die Auslosung von Anfallen durch Karotidenkompression, Wien. klin. Wchnschr. **28**:1422, 1915.

23. Tsiminakis, C.: Die Karotidenkompression bei Epilepsie und Hysterie, Wien. klin. Wchnschr. **28**:1185, 1915.

24. Meagher, R. H., and Ingraham, F. D.: The Relation of the Cervical Sympathetic Trunk to Cerebral Angiospasm, Arch. Neurol. & Psychiat. **22**:570 (Sept.) 1929.

25. Loewy, P.: Schnelldiagnostik der Epilepsie und Hysterie im Felde, Wien. med. Wchnschr. **66**: (July 1) 1916.

26. Wilson, S. A. Kinnier: Modern Problems in Neurology, New York, William Wood & Company, 1929.

27. d'Ormea, A.: Sur les modifications de la circulation cérébrale à la suite de l'administration de quelques essences, Arch. ital. de biol. **40**:141, 1903.

dilatation of the vessels of the brain on the intravenous injection of absinth. However, more recently, Pike, Elsberg, McCulloch and Chappell [28] have reported contraction of the blood vessels of the cortex associated with convulsions due to absinth.

TABLE 1.—*Effect of Injection of Solution No. 1 on Cat 1* *

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	Feb. 1, 1930	3.3	None
Standardization of dosage....	February 9	4.4	One, of 30 seconds' duration
Standardization of dosage....	March 1	4.4	One, of 30 seconds' duration
Standardization of dosage....	March 15	4.4	One, of 30 seconds' duration
Right stellate ganglionectomy	May 1		
Left stellate ganglionectomy..	May 15		
Standard dose.....	May 29	4.4	Three, at 5 minute intervals, of 30 seconds' duration
Subminimal dose.....	June 6	3.3	None

* Male, white and gray cat.

TABLE 2.—*Effect of Injection of Solution No. 1 on Cat 2* *

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	Nov. 9, 1929	4.4	Several, at 5 minute intervals, of 30 seconds' duration
Standardization of dosage....	November 16	3.3	None
Standardization of dosage....	November 23	4.4	Several
Standardization of dosage....	December 7	4.4	Several
Right stellate excised.....	May 6, 1930		
Left stellate excised.....	May 22		
Standard dose.....	June 6	4.4	One, of 1 minute's duration
Subminimal dose.....	June 13	3.3	None

* Female, gray cat.

TABLE 3.—*Effect of Injection of Solution No. 2 on Cat 3* *

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	Dec. 5, 1929	3.3	One, of 1 minute's duration
Standardization of dosage....	December 12	2.2	None
Standardization of dosage....	December 19	3.3	Several, of 30 seconds' duration
Standardization of dosage....	Jan. 9, 1930	3.3	Several, of 30 seconds' duration
Standardization of dosage....	February 4	3.3	Several, of 30 seconds' duration
Right stellate excised.....	March 4		
Left stellate excised.....	May 18		
Standard dose.....	April 1	3.3	Several, of 30 seconds' duration

* Female, black and gray cat.

METHOD

In order to determine whether a relationship exists between angiospasm and epileptiform convulsions, the following experiment was undertaken at the suggestion of Dr. Antoine Schneider.

28. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Chappell, M. N.: The Problem of Localization in Experimentally induced Convulsions, Arch. Neurol. & Psychiat. **23**:847 (May) 1930.

A series of cats was standardized with a convulsant agent. After extirpation of the right and left stellate ganglia, the animals were again subjected to the wormwood oil to see if there was any difference in the effects produced by the standard dose.

TABLE 4.—*Effect of Injection of Solution No. 2 on Cat 4**

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	March 29,1930	5.5	None
Standardization of dosage....	April 5	6.6	One, of 30 seconds' duration
Standardization of dosage....	April 12	6.6	One, of 30 seconds' duration
Standardization of dosage....	April 18	6.6	One, of 30 seconds' duration
Right stellate removed.....	May 6		
Left stellate removed.....	May 22		
Standard dose.....	June 15	6.6	Irritable
Standard dose.....	June 13	6.6	Several
Standard dose.....	November 4	6.6	One

* Female, gray and white cat.

TABLE 5.—*Effect of Injection of Solution No. 2 on Cat 5**

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	Jan. 14, 1930	3.3	One, of 30 seconds' duration
Standardization of dosage....	February 11	2.2	None
Standardization of dosage....	March 6	3.3	One, of 30 seconds' duration
Standardization of dosage....	March 13	3.3	One, of 30 seconds' duration
Right stellate removed.....	April 10		
Left stellate removed.....	April 29		
Standard dose.....	May 13	3.3	One, of 30 seconds' duration
Subminimal dose.....	May 29	2.2	None

* Male, black cat.

TABLE 6.—*Effect of Injection of Solution No. 2 on Cat 6**

Comment	Date	Cc. of Wormwood Oil per Kg.	Convulsions
Standardization of dosage....	Feb. 11, 1930	4.4	None
Standardization of dosage....	March 6	5.5	One, of 30 seconds' duration
Standardization of dosage....	March 13	5.5	Several
Standardization of dosage....	March 22	5.5	One
Right stellate removed.....	May 1		
Left stellate removed.....	May 15		
Standard dose.....	May 29	5.5	Several
Subminimal dose.....	June 5	4.4	None

* Female, tiger-colored cat.

In the standardization of the dose, epileptiform convulsions were induced in six cats by giving them oil of wormwood by means of a stomach tube. The standard dose, established for each animal, was that amount just sufficient to cause a convulsion (at least three different trials) at intervals of not less than seven days. We observed that in animals that had eaten shortly before receiving the wormwood

oil, a dose larger than the standard was necessary to cause a convulsion and that vomiting often resulted. Similar observations were made by Pike and his co-workers.[29] In order that there may be a more rapid absorption of the oil and a full effect obtained, it is administered from about twenty to twenty-four hours after the last feeding. The convulsion occurred usually in from fifteen to thirty minutes.

The wormwood oil solution consisted of 100 cc. of a 3 per cent aqueous solution of gum acacia to which was added 5 cc. of the oil. The same stock solution of the oil was used throughout the experiment for each cat, since various samples of the oil have different degrees of convulsant actions. Two stock solutions were used and are referred to as no. 1 and no. 2.

Excision of the stellate ganglia was performed in two steps. The right ganglion was removed first. Two weeks later, when the animal had sufficiently recovered from the first operation, the left stellate was excised.

Ether was used as the anesthetic, being administered in two cases by means of a tracheal tube and respiration apparatus; in the other four cases a cone was used. In the latter instances particularly, great care was taken to prevent puncturing of the pleura. The following description of the operative technic pertains to the animal when in a supine position, its limbs tied to the operating table. A cushion is placed beneath the back so that the thorax is on a level with or slightly above the level of the rest of the body.

The stellate ganglion is usually found in the thoracic cavity in the interval between the first and second ribs, at the level of the ventral edge of the iliocostalis muscle. A skin incision is made extending at a 45 degree angle from the third rib at the level of the nipple dorsally and cephalad to the level of the caudal border of the first rib. The pectoralis major and minor are split parallel to their fibers, and the axillary fascia is cleared from the region of the first intercostal space. The middle and posterior parts of the scalenus muscle are separated from the underlying serratus anterior. A hemostat is inserted into the serratus just ventral to the long thoracic nerve and just beneath (dorsal to) the dorsal edge of the middle and posterior parts of the scalenus. Immediately ventral to the tendon of the iliocostalis, which is inserted in the first rib, the external and internal obliques are carefully divided. Blunt instruments must be used in separating the fibers of these muscles, as the presence of the intercostal vessels makes the use of sharp instruments hazardous. The ganglion is embedded in a white mass of extrapleural fat. On removal of this fat, the ganglion is seen as a glistening, star-shaped structure. Occasionally, the ganglion lies hidden beneath the second rib. It can then be easily pulled into view. Extreme care is taken to prevent a pneumothorax. If the animal is not too deeply anesthetized, pinching the ganglion with forceps will elicit cries from the animal and will produce dilatation of the pupil. The ganglion is freed from all its branches and the incision closed. This operative technic, as we discovered after working it out, had previously been used by Dresbach and Waddell.[30]

---

29. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Rizzolo, A.: Some Observations on Experimentally Produced Convulsions: The Localization of the Motor Mechanisms from which the Typical Clonic Movements of Epilepsy Arise, Am. J. Psychiat. **9**:259 (Sept.) 1929.

30. Dresbach, M., and Waddell, K. C.: *k*-Strophanthidin Emesis in Cats with Denervated Hearts: The Seat of Its Actions, J. Pharmacol. & Exper. Therap. **27**:9 (Feb.) 1926.

OBSERVATIONS

The typical course of events produced by a convulsant dose is as follows:

1. Period of inactivity: for several minutes after the administration of the oil the cat shows no visible signs of the action of the wormwood oil.

2. Period of distress and restlessness: micturition and defecation may occur; the animal runs about and seeks dark places; the pupils are slightly dilated.

3. Period of extreme sensitiveness: a sudden slight noise, a movement before the eyes or a touch on the skin causes violent muscular twitching; the cat utters loud cries; salivation is profuse, the saliva being of variable viscosity; the pupils are extremely dilated; locomotion is unsteady; there are increased heart rate and dyspnea; the ears feel hot.

4. Period of convulsions: the first sudden violent movement immediately gives way to a state of rigidity in which the whole body vibrates, due to the spasm of both the extensors and the flexors (tonic phase). The rigidity passes into running movements, which at times appear to be well coordinated; the jaws open and close spasmodically; urination often occurs; the hair on the head and back is raised; the pads of the feet are moist; finally a loud gasp may end the convulsion. The animal does not respond to ordinary stimuli either during or a short time after the convulsion.

5. Period of recovery: the pupils return to a normal condition; there is a decrease in the heart and respiratory rates, and the animal gradually subsides to its normal state.

Excision of the stellate ganglion produced conditions that were almost identical in each of the six cats. Contraction of the pupil and protrusion of the nictitating membrane occurred immediately on removal of the ganglion. Drooping of the eyelid occurred invariably. There were excessive lacrimation and sniffling. The pilomotor function of the skin of the head and neck was absent. There were a visible dilatation of the blood vessels of the ear and a marked increase in temperature. These changes took place on the side of the body on which operation was performed.

Removal of the second stellate produced similar changes on the homolateral side. The effects of the first operation were much less marked at the time the second was performed. After the second, the changes observed in both eyes were the same, but the degree of change was greater in the second eye than in the first. This difference persisted for at least five months. The pupils dilated gradually, but even after six months their normal size had not been attained.

About two weeks after extirpation of both stellates the standard dose was administered to the animals. With one exception each cat reacted as before sympathectomy. Cat 4 did not go into convulsions the first time the wormwood oil was administered. Convulsions resulted, however, one and two weeks later when the oil was given. In four cases, a dose just below the standard failed to give a response; in two, a subminimal dose was not administered.

Dilatation of the pupils was less than that seen in normal cats that had been subjected to wormwood oil. The pupils contracted to their former condition within three minutes after the cessation of the convulsions, in contrast to the very slow and gradual return to normal in nonsympathectomized cats. During the convulsions the nictitating membrane receded.

The results might possibly be interpreted to be in accord with those which show that vasoconstriction is not a factor in causing epileptiform convulsions. Because of the many factors involved, a definite statement concerning the significance of the results described is not warranted. The action of wormwood oil may be direct; that is, it may act directly on the walls of the blood vessels of the brain, so that interrupting the path of the sympathetic fibers to the cerebral blood vessels would not prevent vasoconstriction.

SUMMARY

1. Minimal convulsant (standard) doses of wormwood oil were determined for each of six cats.

2. Bilateral stellate ganglionectomy was performed.

3. After recovery the animals were again given the standard dose.

4. Convulsions occurred in the sympathectomized cats which did not differ essentially from those before ganglionectomy.

Clinical Notes

GLIOMA IN THE FOURTH VENTRICLE OF A PREMATURELY BORN INFANT *

MYRTELLE M. CANAVAN, M.D., BOSTON, AND FREDERICK A. HEMSATH, M.D., NEW YORK

In the pursuit of another inquiry, namely, the causation of fetal death, in which the examination of the medullae of the new-born was undertaken to determine the presence of hemorrhages,[1] a certain set of minute histologic observations was selected, and this was adhered to for all the sections. These items were to include a scrutiny of the leptomeninges, the measured width of the vessel walls, the cellular and vascular content of the choroid plexus, the ependyma, the cranial nerve nuclei, the amount of neuroglia (by count in fields) in the substance of the medullae and the amount of myelin at this stage of development; this forms the subject matter of a communication to appear shortly.

This note is to record the discovery, made during the aforementioned histologic search, of a circular body in the fourth ventricle at the midolivary level, springing from the clothing cells of the ventricle. About 80 cells were found in this section resembling those that lay in the subependymal region; the tumor, however, was adherent to the ependyma from which it appeared to arise. No blood vessels were seen in the tiny mass, and there was about as much stroma as there were cells that did not appear to have developed into an adult type.

MacPherson [2] hypothecated that gliomas spring from embryonal rests, and suggested that in any formation there may be an excess of material that can be utilized against the body economy.

The patient, a boy, was a first child; he was born after an estimated nine lunar months of gestation. The labor was short, but the infant breathed with great difficulty; he was cyanotic and did not cry and was unable to expand the lungs properly; he died seven hours after birth.

---

* Submitted for publication, May 27, 1931.

* From the Department of Neuropathology of Boston University School of Medicine and the Department of Pathology of the New York Lying-In Hospital.

1. Hemsath, F. A., and Canavan, M. M.: Microscopic Cerebral Hemorrhages in Stillbirths and Newborn Deaths: A Study of Fifty-Three Infants with Relation to Minute Hemorrhages of the Medulla Oblongata, Am. J. Obst. & Gynec., to be published.

2. MacPherson, Donald J.: Studien über den Bau und die Lokalization der Gliom, mit besonder Berücksichtigung ihres Missbildungscharakters, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **27**:123, 1925.

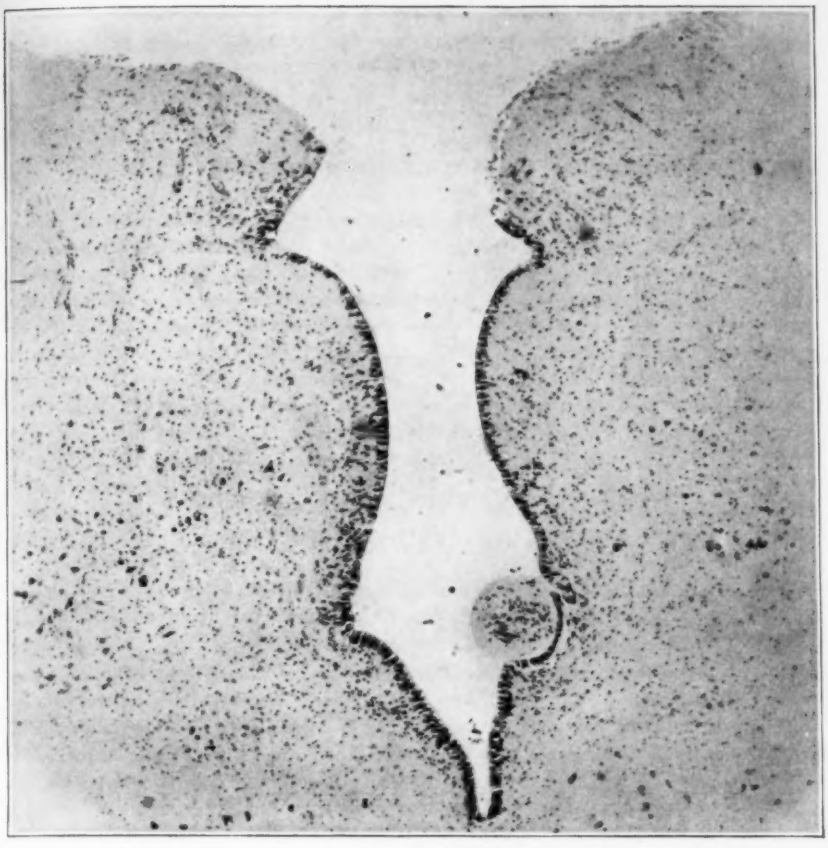

Fig. 1.—Section of medulla showing ependyma lining fourth ventricle, with tumor on the right. Cresyl violet stain; × 120.

Fig. 2.—Drawing of tumor springing from the ependyma, showing type of cell found. Note also the cilia on the ependymal cells, the depth of the cells, the spaces between them and the great number of migrating (?) glia cells beneath the ependyma.

The pathologic conditions noted at autopsy included prematurity, edema of the brain (weight 281 Gm.), relative atelectasis and ecchymosis in the thymus and heart.

We do not claim that the clinical symptoms were dependent on the growth, but report the case as a unique pathologic observation discovered in an intensive search post mortem for hemorrhagic lesions in the medullae of fifty-three stillborn and new-born infants.

CONTINUOUS RHYTHMIC MOVEMENTS OF THE PALATE, PHARYNX AND LARYNX*

NORMAN LESHIN, M.D., AND THEODORE T. STONE, M.D., CHICAGO

Continuous, synchronous, rhythmic movements of the palate, pharynx and larynx were reported in 1886 by Spencer.[1] However, a detailed description of them appeared only when Klien,[2] in 1904, and Freystadtl,[3] in 1928, reported their cases and observations. These movements either may be localized, involving the palate alone, or may include the muscles of deglutition, namely, those of the palate, the pharynx and the larynx. Localized palatal movements are not uncommon, more than 100 cases having been reported. On the other hand, reports of synchronous continuous movements of the palate, pharynx and larynx are rare, only 26 cases having been found in the literature.

The common characteristics of these movements are: they are constant, synchronous, gross oscillatory movements having two phases, a rapid and a slow; they are not related to the pulse or respirations; they persist under anesthesia, and usually are not influenced by extraneous stimulation or the physiologic functions of swallowing and breathing. The movements always occupy the same plane and direction. Their rhythm is constant. The rate is usually between 120 and 180 per minute, rarely below or above these points, remaining constant over long periods of observation. The tempo may vary at times momentarily when a few more rapid movements may intersperse the usual contractions.

The movements of the soft palate are in a vertical plane. The palate rises and falls in each excursion, the elevation being quicker than the depression. Phonation and swallowing, in which the palate is raised, do not interrupt the spasms. The normal movements of the palate and the palatal reflexes are usually intact, with no evidence of any paralysis of the muscles. The posterior faucial pillars in a bilateral involvement approach one another in the midline and then return to their normal positions, the adduction being quicker than the abduction. The rise and fall of the palate give the impression of a curtain being raised and lowered, with the pharyngeal aperture becoming higher and narrower in the first phase and then assuming its natural low and wide position in the second. The posterior pharyngeal wall in the bilateral involvement shows no definite move-

---

* Submitted for publication, Feb. 20, 1931.

* Read at a meeting of the Chicago Neurological Society, Feb. 19, 1931.

* From the Neurological and Otological Service of the Michael Reese Hospital, and the Department of Neurology, Northwestern University Medical School.

1. Spencer: Lancet **2**:702, 1886.

2. Klien, H.: Deutsche med. Wchnschr. **30**:619, 1904.

3. Freystadtl, B.: Kehlkopf und Rachen in Ihren Beziehungen zu den Erkrankungen des Zentral Nervensystems, Berlin, S. Karger, 1928, p. 281.

ment, but gives one the impression that the muscles approach the midline, constricting and narrowing it. In a unilateral disturbance the entire posterior wall moves toward the affected side and back again, the lateral movement being somewhat quicker than the return; the posterior faucial pillar and the palate on the same side are in synchronous motion.

The vocal cords and arytenoids are in continuous motion, approaching one another and then separating, occupying usually for one-third to two-thirds their normal excursion, never meeting in the midline during the spasms. The adduction is slightly quicker than abduction. The movements on one side may be greater than those on the opposite side. The rate is usually the same, and the movements are synchronous with those of the palate and pharynx. The movements may be transmitted to the false cords as well as to the muscles of the aryepiglottic folds. On phonation, the cords move normally, meeting well in the midline, stopping the contractions as long as the cords are held in this position; the spasms immediately commence as soon as the cords are relaxed. The tension of the cords is unimpaired and sensation is normal. In all the cases except 3 (Scheinmann,[4] Porter [5] and Wilson [6]), in which there was a unilateral movement of the palate and pharynx, both sides of the larynx were affected.

The composite picture presented by these synchronous movements is: The quick phase shows the rising of the palate, adduction of the posterior faucial pillars and the arytenoids and vocal cords, followed by a slower movement of these parts in the opposite direction. In unilateral involvement, the rapid phase consists of the lateral movement of the posterior pharyngeal wall toward the affected side, associated with the medial movement of the posterior faucial pillar and the rising of the soft palate on the same side with usually the adduction of both vocal cords and arytenoids. Occasionally there are rhythmic movements of the floor of the mouth, neck and other muscle groups which may or may not be synchronous with the spasms described.

The isolated movements of the palate have practically the same characteristics as those associated with the pharyngeal and laryngeal contractions. In addition, they are usually accompanied by a clicking sound which may be heard when one is close to the patient and which the patient localizes as being present in the ears. According to Valentin,[7] who reviewed the cases of localized palatal contractions up to 1904, these movements usually follow a nervous or mental shock of some sort in emotional, unstable persons who are always conscious of them and seek relief. These movements usually have periods of remission and cease during sleep. Valentin compared these contractions to a habit spasm which may occur as a result of voluntary repetition in children at an early age, later becoming a habit similar to a mental tic.

The first case reported in which these movements were present was by Spencer in 1886. A girl, aged 12, gave a history of a reeling gait, with a tendency to fall backward and to one side, usually the right, intense vertigo, occipital headaches and vomiting for fifteen months. A diagnosis of cerebral tumor was made. Examination revealed an ocular nystagmus having a rate of 180 oscillations per minute. The superior constrictor muscle was moving horizontally and rhythmically as if the posterior pharyngeal curtain were being drawn together. The movements were synchronous with those of the eyes and had a similar rate of 180 per

4. Scheinmann: Vereinsbl. f. inn. Med. **14**:126, 1894.
5. Porter, W. G..: Ztschr. f. Laryng., Rhin. **1**:745, 1909.
6. Wilson, S. A. K.: Brain **51**:119, 1928.
7. Valentin, A.: Ztschr. f. Ohrenh. **46**:84, 1904.

minute. The arytenoid cartilages were also in constant motion, gliding to and from each other. The movements of the cords were interrupted during inspiration and expiration by slight twitches. When the patient stopped breathing the cords gradually closed with from five to six contractions until they finally came close together in a parallel position, resuming their movements again when the respiratory excursions began. No neurologic observations were reported. Spencer termed these movements nystagmus because of their similar rate and synchronous movements with the ocular nystagmus, realizing at the time that it was a slight departure from strict etymologic accuracy.

In 1889, Oppenheim [8] reported 2 cases of this condition. The first was that of a patient with severe occipital headaches, marked vertigo and difficulty in swallowing and speaking. There were paresis and contracture of the left side of the face and contracture of the right extremities. The deep reflexes were increased. There were movements of the left lower part of the face and the platysma. The uvula rose and fell, and the vocal cords adducted and abducted synchronously at a rate of 40 per minute. A diagnosis of epidemic cerebrospinal meningitis was made. In the second case there was a vascular sclerosis, with movements of the head and upper extremities and rhythmic movements of the soft palate and larynx, which had been observed for two months. No other observations were reported. Postmortem examination disclosed a tumor, the size of a hen's egg, in the cerebellum, with pressure on the pons and medulla oblongata and hyperemia and atrophy of the vagus and accessory nuclei.

Scheinmann, in 1894, reported a case of syphilis of the brain with broken down gummas on the posterior pharyngeal walls. A left hemiplegia followed an apoplectic stroke. The right half of the palate was paralyzed. There was a constant rhythmic movement of the left side of the palate, of the posterior pharyngeal wall to the left and of the left vocal cord and arytenoid at a rate of 160 per minute. This was the first case reported of unilateral movements of the muscles of deglutition.

Uckermann,[9] in 1897, reported the case of a man, aged 68, who awoke one morning with loss of speech. He had also twitchings of the arms. The spasm lasted about five minutes and recurred again a short time later. During the next four weeks he was subject to frequent similar attacks. During the attacks there were regular rhythmic movements of the palate, the pillars of the fauces and the vocal cords, which moved from a position of abduction to the cadaveric position. The rate was not reported. At this time he showed increased deep reflexes of the right extremities and weakness of the right arm and leg. A few days later, a lower facial paralysis developed and soon after a violent convulsion of the entire body and head lasting about five minutes. He died a month later, but no postmortem examination was made.

In 1898, Bernhardt [10] reported similar movements in a patient aged 30, who had dull headaches over the vertex and occiput and complained of tinnitus in both ears. This noise was rhythmic and could be heard by the observer when standing near the patient. The noise was associated with rhythmic movements of the soft palate. The faucial pillars, posterior pharyngeal wall and vocal cords were also in rhythmic motion, at a rate of from 100 to 120 per minute, not related to the pulse or respirations. There were no evidences of hysteria or of organic neurologic disease. No diagnosis was made.

---

8. Oppenheim, H.: Neurol. Zentralbl. **8**:132, 1889.
9. Uckermann, V.: Arch. f. Laryng. u. Rhin. **7**:326, 1897-1898.
10. Bernhardt, M.: Deutsche med. Wchnschr. **30**:469, 1898.

Semon,[11] in 1901, reported a similar condition in a woman who kept her head thrown well back with the neck and chin thrust forward, generally inclined to one side or the other, and the mouth slightly open. She complained of clicking noises in the head and curious movements in the abdomen. Two years previously she had localized similar noises in the throat. The sound seemed to be produced by rapid vertical movements of the soft palate with associated similar movements of the floor of the mouth, which continued whether the mouth was held open or closed. However, if the chin was depressed to its normal position, the noises and the movements of the floor of the mouth stopped. She stated at these times that the movements of the palate continued. The arytenoids and vocal cords moved, with equal frequency, energetically from side to side, the movements being occasionally interrupted. At times the movements were so energetic that, during quiet respiration, the inner surfaces of the arytenoids touched one another. The rate was not reported. During phonation everything appeared normal. Memory was good, and there were no other neurologic symptoms. The cause for this condition was not stated.

Steward,[12] in 1903, reported the case of a woman, aged 52, who was suddenly seized with difficulty in speech and inability to walk without assistance. From the onset the symptoms became progressively worse. There were constant slight nodding movements of the head. The palate was constantly moving in alternating quick elevations and slower depressions, varying from 110 to 130 per minute. The vocal cords were also in constant motion, showing two phases, a sharp adduction and a slower abduction. On phonation the cords were brought together in a sudden spasmodic fashion. Movements of the diaphragm were also present. The gait was definitely ataxic, but there was no incoordination of the upper limbs. The knee and ankle jerks were somewhat increased. There was no evidence of increased intracranial tension. Although no neurologic diagnosis was reported, sufficient signs were noted to warrant a diagnosis of organic disease of the central nervous system.

Pegler,[13] in 1903, also reported the case of a woman, aged 20, with rhythmic movements of the palate, upward jerking movements of the uvula and rhythmic adduction of the vocal cords and arytenoids. The rate was noted as being originally from 10 to 15 per minute, and had steadily risen to 240. The patient also complained of entotic tinnitus. When mucus was removed from the nasopharynx, the noise ceased entirely for a time. There was considerable anesthesia of the palate, and when it was held forward with a hook the laryngeal movements continued uninterruptedly. The noises were not heard during sleep. There were no neurologic symptoms in this case, and no diagnosis was reported.

In 1904, Klien[14] reported 2 cases. The first was that of a man, aged 53, in whom paresthesia of the left side of the body, not including the face, developed, with attacks of dizziness. Four months later, he had "crampy feelings" in the left extremities and violent headaches on the right side from which he recovered in three days. The following month left hemiparesis developed, and two months later a partial speech paralysis and a feeling of drunkenness. Since then there had been continuous twitchings of the larynx and frequent "noises in the head." Examination revealed a rhythmic spasm of the muscles of deglutition on the left side only. The spasms were synchronous and strong, with a rate of from

11. Semon, F.: J. Laryng. **16**:131, 1901.
12. Steward, F. J.: J. Laryng. **18**:320, 1903.
13. Pegler, L. H.: J. Laryng. **18**:371, 1903.
14. Klien, H.: Neurol. Zentralbl. **26**:245, 1907.

130 to 160 per minute; they continued uninterruptedly during sleep. The left side of the soft palate was lifted rhythmically toward the left; the posterior pharyngeal wall was drawn to the left; the root of the tongue was raised and drawn over the epiglottis by the left styloglossus, and the muscles of the floor of the mouth were all involved in the rhythmic twitching. A slight twitching of the right side of the face also was noticeable. The muscles of the left aryepiglottic folds and the false vocal cords were also involved in the spasmodic contraction. The vocal cords were synchronously adducted, though the tensor muscles were not involved. The left half of the diaphragm was slightly involved. The spasms were shown most plainly by the muscles of the larynx and the tongue, but only of those that were used in swallowing. The eyelids seemed to twitch slightly synchronously with the throat muscles. The left extremities were very weak, and their movements were slow. There was a tendency on the part of the patient to cry or laugh on the slightest pretext. The patient died during the same year from a self-inflicted gunshot wound of the brain. Postmortem, a small calcified body, 12 mm. in diameter, was located in the left internal capsule. The bullet had made a small opening in the acoustic stria in the lateral part of the fourth ventricle, which involved the middle of the medulla and also the tenth and twelfth cranial nerve nuclei in their entire dorsal quadrant. There was an old lesion of the left upper cerebellar hemisphere extending from the superior horizontal sulcus through the vermis to the dentate nucleus. A second lesion was found at the back of the right cerebellar hemisphere, in the posterior, inferior medial lobe. Microscopically, the superior and middle cerebellar peduncles and the restiform body were degenerated. The contralateral red nucleus was atrophic as was also the left cerebello-olivary tract. There were an increase of glial elements and marked atrophy of the pyramidal cells of the olivary region. Klien stated that there were about one twenty-fifth as many cells as in the opposite normal olive. No involvement was seen in the lower part of the medulla and spinal cord.

Klien's second case was that of a woman, aged 52, who was attacked suddenly with violent vomiting and fell unconscious. She remained unconscious for several hours, and for several weeks was somewhat stupefied. Her speech at first was unintelligible, then recovered gradually, although there remained a lasting defect thereafter. Difficulty in swallowing was at first serious but became less in time. The extremities of the right side were paralyzed, and the patient's face was drawn to one side. Examination showed an advanced sclerosis of the peripheral arteries and a slight hypertrophy of the left cardiac ventricle. All the muscles taking part in the act of swallowing were contracting rhythmically on both sides at a rate of 190 per minute, with no relation to the pulse. Nothing had any effect on the spasms, and they continued during sleep. The muscles of the floor of the mouth and the soft palate, the constrictors, the styloglossi, the thyrohyoidei, the muscles in the aryepiglottic folds, the false vocal cords, the adductors of the vocal cords and the diaphragmatic muscles were all affected. There were also spasms of the intercostal muscles and the muscles of the lower part of the face, synchronous with the throat spasms. The reaction of the pupils was normal. The left eye was open more than the right. The left posterior arch of the palate hung low. In drinking, water would occasionally get into the nasal passages. The tongue deviated slightly to the left and showed a slight atrophy on the left. The right extremities were somewhat paretic, the arm being definitely ataxic and the leg somewhat less so, and the muscles of the shoulder and arm were moderately atrophied. The deep reflexes were more brisk on the right, and there was a positive Babinski sign on that side. There was a slight contraction of the field of vision in both eyes. There were also a left hemianalgesia

and a decrease in the sense of position. Three months later, there developed a left abducens paralysis with a spastic left hemiparesis. On the following day the patient died of pulmonary edema. The autopsy revealed arteriosclerosis of the basal vessels and multiple small foci of fresh and organized softenings in the left half of the brain. These were situated in the internal capsule, caudate nucleus, lenticular nucleus, external capsule, precentral gyrus and middle temporal lobe. The sylvian aqueduct and lateral ventricle were filled with fresh blood. The pons showed an old organized softening. The red nucleus was atrophic, and the pyramidal tracts stained very lightly, the right more so than the left. The right cerebello-olivary tract was markedly degenerated. The left olive was enlarged and degenerated, and showed only one pyramidal cell. The spinal cord was normal.

Sinnhuber [15] also reported a case in 1904. The patient, aged 46, gave a history of double vision and weakness of the left side lasting three weeks. Two years later, he had a transient loss of consciousness with weakness in the right arm and difficulty in speech, which left him with headaches and dizziness. Two weeks later, he noticed movements of the lower part of the face, chin and neck, and that the tip of the tongue pointed to the right. Movements of the palate, pharynx and vocal cords, similar to those already described, were present with a rate of 140 per minute. The pulse rate was from 100 to 120. The movements continued during sleep; the approximation of the vocal cords during phonation was good. No neurologic diagnosis was made.

In 1905, Semon [16] reported a case of a possible tumor of the pons showing these rhythmic movements. A man, aged 27, had received a blow on the right side of the head eight years previously. Four years later, he began to feel giddy and noticed numbness of the left hand from which he recovered. He had several attacks of diplopia and before admission to the hospital complained of weakness in the left arm and leg. Examination revealed an irregular spasm of the soft palate and uvula in a vertical and upward direction, the rate of which was about 150 per minute; it was not absolutely rhythmic, a few quick movements being followed by several slower ones. The pharynx moved in a somewhat oblique direction from the left below to the right above synchronously with the movements of the palate. The entire larynx, except the epiglottis, was affected by a slower spasm similar to that of the pharynx and synchronous with the latter. The cords and arytenoids carried out a series of adduction movements which ranged from abduction to the cadaveric position. A few days later, the patient again developed complete paralysis of the third nerve. No definite diagnosis was made in this case.

In 1909, Porter [5] reported the second case of unilateral movements of the palate and right vocal cord. A man, aged 65, complained of difficulty in swallowing and speaking. He had had a mild apoplectic stroke two years previously which left the left leg somewhat weaker than the right. A second stroke followed one year later. A few months later, the mental state had distinctly deteriorated and he was unable to speak. At this time he had a rhythmic movement of the palate to the right at a rate of about 160 per minute. The right vocal cord and arytenoid showed abrupt rhythmic movements resembling a violent nystagmus, namely, a rapid adduction to the midline and a slower full abduction, which was rather irregular at a rate of 150 per minute. The left vocal cord was quiet except for an occasional slight twitch. On phonation both cords met well in the midline. The neurologist considered that the case was one of bilateral cerebral

15. Sinnhuber: Berl. klin. Wchnschr. **41**:780, 1904.
16. Semon, F.: J. Laryng. **20**:207, 1905.

disease due to arteriosclerosis of the cerebral vessels. The difficulties in deglutition and articulation were to be considered probably as a pseudobulbar phenomenon.

Graeffner[17] reported 2 cases in 1910. The first case was that of a man, aged 70, with pseudobulbar paralysis, who had a continuous clonus of the uvula and larynx. He died a year and a half later. Postmortem examination revealed a large lesion in the right cerebral hemisphere and many smaller lesions in the pons, brain stem and cerebellum. The second case was that of a woman, aged 65, who had had frequent brain insults with a speech disturbance, asymmetry of the face and an abnormal position of the body similar to that of paralysis agitans. Examination revealed the left side of the palate and the uvula in continuous rising and falling movements at a rate of 110 per minute. The arytenoids and vocal cords were also in motion, synchronous with those of the palate, the right moving more than the left. The patient was not conscious of these spasms. The pulse rate was 76. She also had a coarse tremor of the tongue, which was atrophic on the right side.

Graeffner also cited a case of Liepmann's[18] of a syphilitic patient, aged 32, who had had several apoplectic attacks during the preceding year. He had rhythmic movements of the palate and vocal cords, the left more than the right. There was no paralysis of the vocal cords.

Klien,[19] in 1918, reported 2 more cases, making 4 in all that he had seen. The first was that of a man, aged 42, who had had frequent dizzy spells and an apoplectic insult with paresis of the right leg three years previously. Following this his speech became more difficult, and a year later double vision developed. Examination showed a weakness of the right leg, which was slightly ataxic. The right patellar and achilles reflexes were stronger than those on the left. He also had a positive Babinski sign on the right. There was no adiadokokinesis. The typical rhythmic movements of the muscles of deglutition were present on the right at a rate of from 140 to 170 per minute. The muscles of the floor of the mouth, the pillars and the elevators of the larynx were similarly involved. Both vocal cords were in abduction and adduction synchronous with the other movements. The right false cord moved also, but not the left. On phonation, the left cord moved slightly over the midline. These movements continued until death, which occurred several weeks later following the development of ataxia of the left arm, astereognosis and strong lateropulsion toward the left.

Postmortem studies of the brain showed fresh hemorrhages in the right cerebral hemisphere. One hemorrhage was in the rolandic area, in the outer capsule, involving two thirds of the lenticular nucleus; it had broken through behind into the ventricle. Another old hemorrhage was found on the boundary between the middle and lower third of the ascending frontal convolution immediately above the supramarginal gyrus and the parietal lobe, extending backward to the frontal plane of the tip of the posterior horn. The left cerebral hemisphere showed an old hemorrhagic cyst, the size of a pea, in the parietal lobe about the lenticular nucleus. In the middle and outer portion of the lenticular nucleus was another small hemorrhagic cyst. The cerebellum and brain stem, on microscopic examination in serial sections, showed cause for the movements of the musculature involved in swallowing on the same side, namely, the right. The dentate nucleus in its posterior and under surface was involved, and the external

17. Graeffner: Berl. klin. Wchnschr. **47**:1081, 1910.

18. Liepmann, H., cited by Graeffner (footnote 17).

19. Klien, H.: Monatschr. f. Psychiat. u. Neurol. **43**:79, 1918.

surface of the medulla oblongata was similarly affected. The brain stem in the same region was involved through the ventricular hemorrhage. The remainder of the brain stem and medulla oblongata was unaffected.

The other patient was seen only once. The case was one of arteriosclerosis, with a history of several apoplectic attacks. The neurologic picture was that of a pseudobulbar paralysis with continuous, rhythmic movements of the palate, pharynx and larynx.

In 1918, Kelly [20] reported a case in which there were nystagmoid movements of the posterior lateral wall, left tonsillar region and left half of the soft palate. The laryngeal twitchings were present during respiratory movements, greatest at the left vocal process and left arytenoid. The right half of the larynx was affected to a less degree. On phonation, the cords approximated well and the movements stopped. Postmortem examination, two years later, showed that the previous mental state was due to cerebral arteriosclerosis and softening, and that death had resulted from hemorrhage into the cerebellum with pressure on the pons and medulla. Capillary fibrosis was particularly marked in the cerebellum. The superior cerebellar arteries were thrombosed, but, owing to compensatory anastomosis through the inferior arteries, gross extensive softening had been prevented in the cerebellum.

Pfeiffer,[21] in 1919, reported the case of a soldier who, five months previously, had received a shrapnel shell wound in the left occiput, about 3 or 4 cm. behind the mastoid process, with injury to the underlying brain. At an operation, a month later, pus, splintered bones, and a prolapse and pulsation of the brain were found. Ten days later, the prolapse subsided and the pulsation was no longer present. Two months later, the wound was entirely healed. Later, he complained of weakness in the left arm and leg. Examination revealed weakness of the left hand. The reflexes were equal on the two sides, and the Babinski test was negative. There was a horizontal ocular nystagmus when looking to the right and a rotary nystagmus on fixation to the left. There was also a right facial weakness, with nystagmoid movements of the soft palate and posterior pharynx that were constant and synchronous. The patient also complained of dizziness when turning the head to the left. Six months later, he showed difficulty in walking, with a tendency to fall to the left. The Romberg test gave negative results. Hemiataxia was present on the left side. There were rhythmic movements of the nasopharynx and the palate, and synchronous movements of the left false and true cords, all at a rate of 140 per minute. Phonation showed the vocal cords to be normal. The history and results of examination strongly suggested a left cerebellar lesion.

Bloch and Lemoine,[22] in 1926, reported the case of a man, aged 54, who had a right hemiplegia and two days later developed a quadriplegia with a typical pseudobulbar syndrome. Six months later, he showed typical signs of cerebellar disease in addition to the pseudobulbar paralysis. Examination, in addition to the typical neurologic signs characteristic of these conditions, showed a continuous rhythmic spasm of the palate, pharynx and larynx. No detailed description of the movements or their rate is given.

In 1928, Freystadtl [3] reported 3 cases. The first was that of a woman, aged 58, who, ten months previously had had an attack of dizziness without loss of

---

20. Kelly, A. B.: Proc. Roy. Soc. Med. (Laryng. Sect.) **11**:140, 1918.

21. Pfeiffer, R. A.: Monatschr. f. Psychiat. u. Neurol. **45**:96, 1919.

22. Bloch, A., and Lemoine, J.: Ann. d. mal. de l'oreille, du larynx **45**:1056, 1926.

consciousness. Examination showed a general weakness with no paralysis. Her speech was not intelligible. Six weeks later, her ability to appreciate what was said to her was worse, and she began having attacks of severe dizziness. For two months the right hand had trembled and dizziness was severe even when she was lying down. The pulse rate was 120, and the blood pressure 220 systolic and 185 diastolic. Examination showed the pupils to be normal, with proper reaction to light and in accommodation, and small vertical, horizontal and rotary movements of the eyeballs. There was no involvement of the cranial nerves. The deep reflexes on the right were greater than on the left with a positive Babinski test on the right. The abdominal reflexes were not constant. She had also a right spastic paralysis with some atrophy of the right forearm and the right interossal muscles. There was a marked cerebellar ataxia. The Wassermann reaction was negative. The soft palate, posterior pharyngeal wall and vocal cords were in continuous rhythmic contractions, from 140 to 160 per minute, all synchronous and at the same rate. The movements were biphasic. There was no impaired mobility of the palate. Psychic influences affected the amplitude of the movements, increasing their excursions and making them temporarily arrhythmic. There were also rhythmic contractions of the right angle of the mouth, the neck, the intercostal muscles, the abdominal wall and the eyelids, and ocular nystagmus. All these movements were weaker and less frequent than those of the pharynx and larynx. The neurologic signs were compatible with a picture of a multiple vascular sclerosis.

The second case was that of a woman, aged 61, who, two years previously, had had an apoplectic stroke in which the left side of the face and the left upper extremity became paralyzed in association with a speech difficulty. The patient later developed greater impairment in speech, with attacks of laughter and crying. Dizziness became so severe that the patient required rest in bed. The heart was enlarged to the left, and the aorta was dilated. The pupils were normal. There were no nystagmus, paralyses or disturbances of sensation. The deep reflexes were increased on the left. She had tingling sensations in the left side of the face and the left upper extremity. The Romberg test gave positive results. Examination of the pharynx and larynx showed a tremulous tongue and a clonic spasm of the soft palate. The left half of the palate elevated itself less than the right. The vocal cords were in continuous adduction and abduction movements, the abduction being more rapid than the adduction. All movements of the swallowing apparatus were synchronous, with a rate of 140 per minute.

The third case was that of a butcher, aged 34, who had suffered from alcoholism for the preceding two and one-half years. One morning he noticed that he could not move his right arm and leg, and that tingling was present in these limbs. He was unable to stand for five weeks after the attack. Speech difficulty was present with the paralysis. The blood pressure was 100 systolic and 75 diastolic. Examination showed the pupils to be normal, and a rotary nystagmus when looking to the left. There were paralysis of the lower right side of the face and ataxia of the left upper extremity. He walked like a drunken man. The right deep reflexes were increased, with a right knee and ankle clonus and a positive Babinski test. The abdominal reflexes on the right were diminished. He had marked hypotonia and a diminished patellar reflex on the left. There was ataxia in all the extremities with an intention tremor of the hands and adiadokokinesis. There was also a thermal paresthesia in the right half of the body, with sensations of cold. Examination of the pharynx and larynx revealed clonic movements involving the posterior pharyngeal wall, the vocal cords and the palate, with a rate of from 124 to 126 per minute. The movements had a fast and slow component. They did not interfere in any way with the patient's ability to eat, speak or

swallow. The changes on the left side in this case were due to a lesion in the cerebellum. All the observations might have been due to an embolus or trauma associated with an alcoholic background.

Wilson [6] also reported a case in 1928. A man, aged 53, complained of weakness of the left arm and leg, failing sight and a bad memory for two years. The onset had been sudden. Three months previous to the examination, he had had a severe headache and suddenly became blind. Eyesight gradually returned after two months. A week later he had a right-sided convulsion followed by hemiplegia. Speech was lost for three days. Examination revealed defective mentality and bad memory in a man who cooperated poorly but seemed to be well oriented. The reaction of the pupils was normal. The limbs were weak, and their muscle tone was increased. The reflexes were exaggerated but equal in the upper extremities. The abdominal reflexes were sluggish in the upper, and absent in the lower, quadrants. Both knee and ankle jerks were exaggerated with bilateral ankle clonus but no Babinski sign. The blood pressure was 190 systolic and 112 diastolic. The palatal movements were in a vertical direction, regular in rate; at first they occurred at a rate of 144 per minute but later decreased to 116. There was a horizontal nystagmoid movement of both superior constrictor muscles, especially the left, and of the left posterior faucial pillar. The palate moved poorly but equally and symmetrically, and the palatal reflex was normal. The larynx showed well marked twitchings of the left arytenoid and vocal cord, synchronous with those of the palate. There were no involuntary movements on the right side. Examination of the spinal fluid revealed a very slight increase in the protein content only. This is the third case reported showing unilateral laryngeal movements in unilateral involvement of the palate and pharynx.

REPORT OF CASE

History.—J. T., a Roumanian Jew, aged 42, a tailor, had been entirely well until five years before when weakness gradually developed in the left leg. He described it as if the leg would go from under him. Walking was difficult in cold weather and on slippery surfaces. The condition improved somewhat until about two and one-half years before when he again developed difficulty in walking which he described as limping or dragging of the left leg. A short time later, he suddenly became dizzy and fainted, falling down a flight of eight stairs; he remained unconscious for about fifteen minutes. On awakening he discovered weakness in the left arm, and the leg was considerably worse, walking being more difficult. He was unable to extend the left arm fully and noticed clumsiness, especially in the left hand, to such an extent as to make threading a needle or buttoning his clothes very difficult. The condition of the left arm and leg became progressively worse so that at the time this article was written walking was extremely difficult; he required a cane for support.

About two years before examination, a coarse tremor of the left hand and leg developed. The tremor was made worse by an attempt at movement. For the past year, the patient had become more sensitive to cold. His vision had become blurred, and reading had been difficult. He had never had paresthesias or numbness. The family history was without significance. The past history of the patient was without significance except for some difficulty with urination for the past sixteen years, either in starting the stream or from dribbling after urination. Complete incontinence of urine or feces had never been present. He also had a trigeminal neuralgia which had been successfully injected with alcohol sixteen years previously. Tinnitus had been present in the right ear for the past seven years.

Physical Examination.—There was no objective evidence of physical disease. The blood pressure was 115 systolic and 75 diastolic in the left arm and 118 systolic and 76 diastolic in the right; the pulse rate was 78, and the respiratory rate, 20.

Neurologic Examination.—There was a hemiparesis on the left, including the face and tongue; the latter protruded to the left. The left upper extremity showed many postplegic hyperkinetic movements that resembled dystonia. The left lower extremity was markedly spastic and ataxic. The right upper extremity was not ataxic, while the right lower was moderately ataxic. The knee, ankle, triceps, biceps and wrist jerks were bilterally brisk, those on the left being more brisk; the abdominal and cremasteric reflexes were absent on the left, while the former were present and the latter diminished on the right; the Babinski sign was present on the left, while the Chaddock, Gordon, Oppenheim and Mendel-Bechterew-Strümpell signs were bilaterally absent; ankle clonus of an inexhaustible type was present on the left. Proprioceptive pain and temperature senses were normal. The sense of taste was normal. The eyeballs revealed spontaneous nystagmus when looking to either side and upward. There were a coarse horizontal nystagmus to the right when looking to the right, a mixed horizontal and rotary nystagmus of a less degree on fixation to the left, and a slight vertical nystagmus when looking upward. The left optic fundus showed a slight pallor of the temporal half of the disk; the pupils were unequal, the right larger than the left; both reacted sluggishly to light and normally in accommodation. The left nasolabial fold was less marked than the right; the tongue was coarsely tremulous and protruded to the left. There were slight twitchings of the left angle of the mouth, chin and left platysma muscle, rhythmic and synchronous with the movements of the pharynx to be described. The remaining cranial nerves, with the exception of those supplying the palate, pharynx and face, were entirely normal.

Examination of hearing showed both ears to be within normal range for the unaccentuated whispered voice and the tuning forks, except for a slight diminution for the lower tones. The Rinné, Schwabach and Weber tests were all within normal limits. Complete examination of the vestibular apparatus by the rotation and caloric tests revealed that the peripheral labyrinthine system reacted normally in all respects.

Examination of the pharynx revealed the entire posterior pharyngeal wall in continuous rhythmic to and fro movements to the left in a horizontal plane. The movements had two components, a slightly quicker movement to the left and a slower one returning. The rate taken repeatedly at various times was always 132 per minute. The rhythm always remained the same, but the tempo would vary occasionally, especially with manipulation of the tongue, when a few quicker movements would interrupt the regular ones. Laughing, swallowing or phonation did not interrupt the oscillations. The muscles of the posterior wall of the nasopharynx and hypopharynx were similarly involved. The left posterior faucial pillar was also in rhythmic motion, moving toward the midline and back again, synchronously with the movements of the pharyngeal wall and at the same rate. Here also the movements had two phases, the excursion medially being somewhat faster than the returning lateral one. The excursion of the pillar transmitted slight movements of the palate, especially on the left side, which seemed to rise and fall. The uvula, which pointed slightly to the right, showed a rather rotary swinging motion backward and upward. All these movements were synchronous, at the same rate, with slight transient variations in tempo, composed of two components, with no relation to the pulse or respiration. The movement of the pharynx to the left was accompanied by the excursion of the left posterior pillar to the right toward the midline, giving one the impression that the pillar was pulling the pharyngeal wall toward

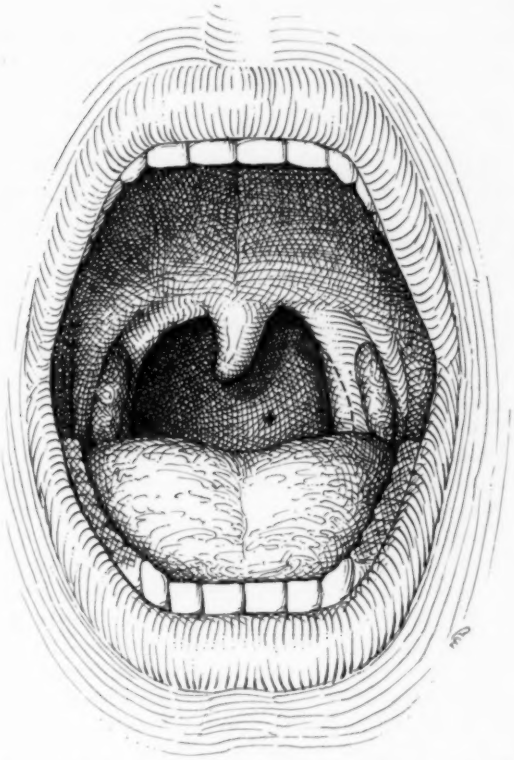

Fig. 1.—Palate and pharynx at the end of the first phase of the movement, showing the palate raised, especially on the left side, the uvula pointing to the right and raised upward and backward, the pharyngeal aperture higher and narrower, the posterior pharyngeal wall moved to the left, and the left posterior faucial pillar moved toward the midline.

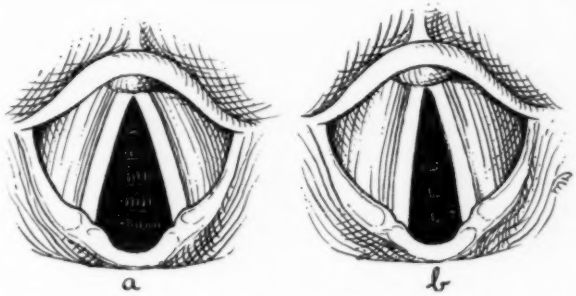

Fig. 2.—The vocal cords and arytenoids in the (*a*) abduction phase and the (*b*) adduction phase of the movement.

the left around some fixed point. At the same time there was a slight elevation of the palate and the uvula (fig. 1). The return movements were together also, in the opposite direction. The normal movements of the palate and the palatal reflex were not impaired. When elevated the palate deviated slightly to the right. The sensations in the palate and the pharynx were not diminished.

Examination of the larynx made indirectly, using the laryngeal mirror, showed both vocal cords and arytenoids in similar rhythmic motion. The cords and arytenoids approached each other and then returned, the movements occupying only approximately one-third their normal excursions, never meeting in the midline during these oscillations (fig. 2). The movements also had two phases, the adduction being quicker than the abduction. The right vocal cord and arytenoid moved more than those on the left. The rate was also 132 per minute, but the regularity seemed to vary more than in the pharynx. The smaller excursions interspersed the regular ones more frequently, and at times those on the left appeared to stop entirely for a brief pause. During the regular tempo, the laryngeal oscillations seemed to be synchronous with those of the pharynx, the adduction of the cords and arytenoids occurring at the same time as the movement of the pharynx to the left and of the left posterior pillar to the midline. Slight movements were also present in the false cords and both aryepiglottic folds, especially the right. The normal movements of the vocal cords and arytenoids were unimpaired, meeting in the midline during phonation and showing no evidence of paresis or changes in tension. The respiratory movements did not affect the rhythmic oscillations. During phonation the movements stopped and the cords remained quiet as long as they were held in the midline, resuming their rhythmic excursion as soon as they were permitted to open. The movements of the larynx could be felt by placing the finger on the neck in the notch of the thyroid cartilage.

The patient was not conscious of any of these movements. They did not interfere in any way with the physiologic functions of swallowing, speaking and breathing. The movements were always present, even during anesthesia, as was seen when the patient was under ether narcosis for esophagoscopy. The movements of the pharynx, pillar, palate and larynx were exactly the same as when the patient was conscious. An esophagoscopy was done (Dr. S. J. Pearlman) to determine whether the movements involved the muscles of the esophagus. No involvement was present. The nasopharynx was also examined with the nasopharyngoscope. Rhythmic movements were seen on the left lateral wall, referred from the left posterior pillar. There was a suggestion of a slight movement of the outer lip of the eustachian tube, with no opening and closing contractions at the opening of the tube. The right lateral wall of the nasopharynx showed no movements.

Laboratory tests showed that the blood had 4,560,000 red cells, 8,300 white cells and 80 per cent hemoglobin; the differential white count was 65 per cent polymorphonuclear cells, 35 per cent lymphocytes, 1 per cent eosinophils and 2 per cent monocytes. Chemical analysis of the blood revealed: blood sugar, 69 mg., and nonprotein nitrogen, 33 mg. per hundred cubic centimeters of blood. The Wassermann and Kahn reactions of the blood were negative. The urine was entirely normal. The spinal fluid was clear, under a pressure of 12 mm. of mercury, with no evidence of subarachnoid block; there were only 2 cells, with a negative test for globulin. The Wassermann and Lange reactions were negative.

A diagnosis of multiple sclerosis was made.

COMMENT

By far the majority of cases reported in the literature we have surveyed were due to organic disease of the central nervous system. In the twenty-seven cases

reported, including our own, sufficient evidence was present in twenty-four instances to make a diagnosis of disease of the central nervous system. The remaining three cases, those of Bernhardt, Semon and Pegler, are not included in this group because of insufficient reports of the neurologic condition. Of the twenty-four cases showing evidence of organic disease, nineteen showed positive evidence of cerebellar dysfunction. The six cases in which a postmortem examination was made presented cerebellar disease in addition to cerebral involvement. Klien, in his three cases examined post mortem, found a left-sided spasm in a left cerebellar disease, a right-sided involvement in a right cerebellar disease and bilateral movements with bilateral cerebellar involvement. Fourteen of twenty-seven cases in our series showed cerebral arteriosclerosis; in three instances there was sufficient clinical evidence to make a diagnosis of bulbar palsy.

Cases of isolated spasm of the palate have been reported in which some infection or irritative process has been found in the nose, the nasopharynx or the ears, which ceased after treatments applied to these areas. These cases were found in persons who had a neurosis. Two cases have been reported in which the movements of the posterior pillars, arytenoids and vocal cords were influenced by local treatments. Pegler reported the case of a woman, aged 30, who complained of noises in both ears. Examination revealed the movements at a rate of 42 per minute. She also had an intumescence of the inferior turbinates. Following cauterization the noises were greatly diminished, and the rate of the movements was less; no mention was made that they were entirely diminished after the treatments. The woman was nervous. Labat [23] also reported a case in a girl, aged 20, who had an influenzal aphonia with movements of the vocal cords. These ceased following permanent relief from the hypertrophy of the inferior turbinates. In neither case was the rate of the pulse or respirations noted, nor were the neurologic signs mentioned. In the case of Labat the movements were localized in the larynx and were called choreiform spasms. It does not seem possible to us that any local disease can produce these synchronous movements unless it is marked and extensive. Practically all the cases showing these movements contain reports of no evidence of disease in the palate, pharynx or larynx. Hypertrophy and intumescence of the inferior turbinates, mentioned in the two cases as a possible etiologic factor, are very common and should therefore have produced a greater number of cases of this symptom complex than we have been able to find in the literature. In many of the cases reported in our review, including our own, the authors stated that cocainization of the parts involved had no effect on the movements.

Spasms of a similar nature have been described in hysteria. Ernst [24] reported a case of similar rhythmic movements in the palate, pharynx and larynx synchronous with contractions in the epigastrium at a rate of from 52 to 56 per minute following local injury to the larynx. The contractions of the vocal cords differed in that they were not held tense, and the epiglottis at the same time showed definite bending movements. The only neurologic evidences of analgesia and themo-anesthesia involving the entire trunk and upper extremities were not compatible with an organic lesion. Schultzen [25] also reported a case of rhythmic movements of the arytenoids and vocal cords in a man, aged 27, following a severe contusion of the thorax. These movements were always associated with the respirations, which were

23. Labat, F., cited by Rethi, L.: Die laryngealen Erscheinungen bei multipler Sklerose des Gehirns und Rückenmarks, Vienna, Josef Safár, 1907, p. 113.

24. Ernst, E.: Neurol. Zentralbl. **26**:954, 1907.

25. Schultzen: Charité ann. **19**:169, 1892-1893.

usually between 50 and 70 per minute. Baginsky [26] reported a case in which only laryngeal movements were present, synchronous with the respiratory excursions. Boeck [27] reported a case in which the movements of the palate and larynx were synchronous with the pulse, and which stopped following three electrical treatments of the mastoid. It is evident in these latter cases that the frequency was much less than that found in cases with an organic etiology. We believe that hysterical clonus should offer no difficulty in differential diagnosis. In hysteria the movements are not constantly regular, but tend to be irregular; they disappear usually when the attention of the patient is drawn to something else; they may be synchronous with the pulse and respiration so that their rate is less than that found in the organic cases; there are no objective evidences of organic disease of the central nervous system; there are other signs of neuroses such as hysterical anesthesia, hyperesthesia and paralysis, and voluntary effort will usually stop the spasm.

SUMMARY

A complete review of twenty-six cases found in the literature is given in detail.

A case is reported showing continuous rhythmic movements of the palate, pharynx and larynx. Neurologic examination revealed objective evidence of organic disease of the brain and cerebellum. A diagnosis of multiple sclerosis was made.

DISCUSSION

DR. ROBERT SONNENSCHEIN: In these days of high development of specialization it seems an act of supererogation for a mere laryngologist to attempt to say anything on a neurologic subject. However, I had the privilege of reading this excellent paper of Dr. Leshin and Dr. Pearlman, my associate, and enjoyed seeing the pictures. I know little about the subject. We attempt by means of the vestibular test to aid in diagnosing some of the neurologic phenomena. I have never before seen a case of this type, but I am not surprised when there are only twenty-six on record. I saw this patient while he was in the Michael Reese Hospital. The paper emphasizes the need for cooperation between otolaryngologists and neurologists.

DR. G. B. HASSIN: Can Dr. Stone suggest the part of the brain, medulla or cerebellum responsible for the movements? When I looked at the motion picture, I thought first that a lesion of the pyramidal tract caused the hyperkinetic phenomena in the parts supplied by the tenth nerve. However, the movements of these parts (uvula and vocal cords) are not unlike those seen in similar movements in the tongue observed in postencephalitic states. They suggest the possibility of an extrapyramidal lesion, especially because in one of the cases referred to by the essayist the red nucleus was involved—a part of the extrapyramidal system. Since this is the case, vascular lesions in the form of multiple foci of softening would probably be suggested rather than multiple sclerosis, in which hyperkinesia of the larynx and pharynx is not known to occur.

DR. LEWIS J. POLLOCK: In connection with the possibility of vascular lesions as opposed to multiple sclerosis, it is well to note the history in relation to the absence of apoplectiform attacks, except when there was an increase of an already existing disability of the leg following the vertiginous attack and loss of consciousness. Although the vertiginous attack speaks for a vascular lesion, I find it difficult to correlate the symptoms in this case with those hitherto reported as being due to a vascular pathologic process. The exacerbations, remissions and progressive increase of disability over considerable periods of time support this.

26. Baginsky, A.: Berl. klin. Wchnschr. **28**:1175, 1891.

27. Boeck, O.: Arch. f. Ohrenh. **1**:267, 1867.

ENCEPHALITIS WITH UNUSUALLY HIGH EOSINOPHILIA *

MILTON G. BOHROD, M.D., ARTHUR F. GOODYEAR, M.D., AND O. O. STANLEY, M.D.,
DECATUR, ILL.

The following case is reported because of the unusually high eosinophilia in what is apparently a case of encephalitis. While eosinophilia is not uncommon in cases of encephalitis that end in recovery, it is usually only moderate; so far as we know, the extreme degree observed in our case has never been recorded.

REPORT OF CASE

History.—A white man, aged 37, complained on March 14 of excruciating pain extending from the middorsal spine to the left scapular region and down the left arm. He thought that it was caused by a shrapnel wound in the left shoulder received in the World War. Ten days before, while on a business trip, he had eaten some chop suey; following this he had had a severe gastro-intestinal disturbance with diarrhea lasting about three days. Since that time his bowels had been rather sluggish. There was nothing of significance in the past history. He had pyorrhea, with marked retraction of the gums. The temperature was 98.2 F., the pulse rate 74, the respiration rate 14 and the blood pressure 128 systolic and 80 diastolic. The heart and lungs were normal. All the reflexes were normal. Urinalysis gave negative results. No improvement occurred in the next few days. On March 19, the patient became exceedingly restless and complained of insomnia. Two days later, he was unable to use the right hand and shoulder, and had to be assisted in dressing. On March 22, he became very restless, cried and was mentally confused. There was a flushing of the face, especially about the eyes and nose. He was sensitive wherever touched. He seemed unable to get out of bed or to use the right arm. He was sent to the hospital.

Examination.—On his admission to the hospital, the patient's temperature was 98.2 F., the pulse rate 84 and the respiration rate 22. He was very restless and unable or disinclined to answer questions; he tossed about in bed, but seemed to recognize people about him. The pupils were equal and regular, and reacted to light and in accommodation. The movements of the eyes were adequate in all directions. The gums were soft and spongy, and the teeth were in a poor condition. The heart and lungs were apparently normal. There were no palpable masses in the abdomen, and no tenderness or rigidity. The upper extremities were slightly spastic. The gastrocnemius muscles were decidedly tender. The abdominal reflexes were absent. All other reflexes appeared to be normal. The urine was normal. A blood count made on the next day disclosed: red cells, 4,720,000; hemoglobin, 95 per cent; white cells, 16,750; neutrophils, 36, lymphocytes, 11, monocytes, 2, basophils, 0.5, and eosinophils, 50.5 per hundred cubic centimeters. Spinal puncture revealed an increased pressure; there was no globulin; there were 5 cells per cubic millimeter. The Kahn test was negative and the colloidal gold curve normal. Cultures of the fluid remained sterile.

Diagnosis.—At this time the diagnosis of a cerebral disturbance, probably encephalitis, was strongly considered. However, a history of gastro-intestinal dis-

* Submitted for publication, March 20, 1931.

* From the Pathology Laboratory and the Medical Service of the Decatur and Macon County Hospital.

turbance ten days previously, following the eating of chop suey, the muscular tenderness and especially the very high eosinophilia led to a provisional diagnosis of trichinosis. Repeated examinations of the tools, urine, blood and spinal fluid failed to disclose parasites of any kind.

Course.—On March 27, a biopsy of the left gastrocnemius muscle was performed. No trichinae were found, but other changes were evident. The striations, especially the transverse ones, were indistinct, and in places the muscle was almost hyaline. Around some of the blood vessels and between the muscle fibers there were accumulations of cells, predominantly lymphocytes, but with considerable numbers of neutrophilic and eosinophilic leukocytes.

On March 28, the patient developed peculiar petechial hemorrhages underneath all the finger-nails, parallel to and about from 1 to 2 mm. behind their free margins. One of the nails with the underlying tissue was removed, but sections showed only hemorrhages. No parasites or infiltrations were seen. There were no other petechial hemorrhages anywhere on the body.

Observations on the Blood in the Case Reported

Date	Hemoglobin (Sahli) per Cent	Red Blood Cells	White Blood Cells	Neutrophils	Eosinophils	Basophils	Neutrophilic Myelocytes	Eosinophilic Myelocytes	Lymphocytes	Monocytes
3/26	95	4,720,000	16,750	36.0	50.5	0.5	...	...	11.0	2.0
4/ 1	71	4,410,000	13,000	54.0	28.5	0.5	3.0	...	13.5	0.5
4/ 4	90	4,760,000	7,900	44.5	29.5	1.0	2.5	...	17.0	5.5
4/11	85	5,530,000	16,650	47.0	25.0	...	...	...	28.0	...
4/18	77	4,660,000	13,700	41.0	23.0	1.0	...	9.0	22.0	4.0
4/25	88	5,030,000	9,950	43.0	19.0	1.0	...	3.0	28.0	6.0
4/30	84	4,700,000	10,000	43.0	23.0	...	...	2.0	30.0	2.0
5/ 9	80	4,470,000	11,900	46.0	24.0	...	...	...	29.0	1.0
5/16	97	4,640,000	10,200	54.0	22.0	1.0	...	...	20.0	3.0
6/11	100	5,110,000	10,600	47.0	17.0	...	1.0	1.0	31.0	2.0
7/23	104	4,790,000	8,850	42.0	4.0	2.0	...	...	52.0	...
11/ 4	..	.....	10,050	58.0	2.5	...	...	...	38.5	1.0

On March 31, the patient's restlessness became more marked, and it was noticed that he did not use the left hand or arm. All the reflexes in this arm were absent. So far as could be determined, sensation seemed to be intact. During that night the arm became spastic for a short time, but then it became flaccid and remained so for many days. On April 3, spinal puncture was repeated; the pressure was still increased, but there was no globulin, and there were only 2 cells per cubic millimeter; no parasites were found. The spinal fluid sugar was 92 mg.

The restlessness continued until about April 8. Toward the end of this time the patient had lucid periods during which he realized that he had had what he called a "terrible mental condition." From that time the mental state gradually cleared, except for occasional days during the next two weeks, when the old restlessness and mental confusion returned. The use of the left arm and hand returned much more slowly, and it was not until about two months later that the patient was able to feed himself comfortably, and still longer before he was able to perform skilful movements with that hand.

During this time the temperature remained about normal. On several occasions it reached 100 F., but for the most part varied between 98 and 99.5 F. The pulse rate occasionally reached 110, but remained normal most of the time. Respiration was always normal.

Blood Examinations.—A summary of the important observations on the blood, studied over a period of several months, is given in the accompanying table. The

number of red cells and the hemoglobin content were consistently normal. The number of white cells showed considerable variation during the first two weeks (from 7,900 to 16,700), but for the most part was at a high level, which gradually came down. During the early part of the illness the neutrophilic leukocytes were increased in number. Myelocytes were found on several occasions, up to 3 per cent. The outstanding abnormality was the unusually high eosinophilia, which was 50.5 per cent at the first examination, then remained between 20 and 30 per cent for about two months, and during the next two months gradually declined, to become normal four and one-half months after the onset of the illness. About the third week of the illness, a large number (9 per cent) of eosinophilic myelocytes appeared in the peripheral blood; the number gradually decreased, and they disappeared when the eosinophilia was over.

On May 12, a third biopsy, this time of the deltoid muscle, was performed. The muscle appeared perfectly normal; no trichinae were found. Roentgen examination of the muscles of the shoulders disclosed no calcified areas.

Condition Seven Months After the Onset.—The patient is able to work all day, although he occasionally becomes tired toward the end of the day. There is a definite fixity of the facies, especially noticeable about the mouth and eyes, and speech is slow and tends to be in a monotone. There is slight rigidity of a cogwheel character in both arms. The face gives the definite appearance of a mild parkinsonism.

COMMENT

Eosinophilia is so common in parasitic infections that in every case in which it is marked animal parasites should be sought. In our case the history suggested trichinosis. The history of a gastro-intestinal upset following the eating of chop suey, the muscle tenderness and the eosinophilia pointed toward the possibility of this condition. Even the appearance of encephalitis did not exclude this diagnosis, for encephalitis due to trichinae has been reported.[1] However, the persistent absence of parasites in three biopsies and the absence of parasites in the stools, blood and cerebrospinal fluid make this diagnosis, while not impossible, at least highly improbable.

The neutrophilic leukocytosis of acute infectious diseases has also been found in most cases of encephalitis.[2] Yet there has repeatedly been mentioned a tendency for encephalitis, more than for most other acute infectious diseases, with the exception of scarlet fever, to be accompanied by eosinophilia, especially in cases with a good prognosis.[3] Thus, it has been found that, while in fatal cases the eosinophils are markedly reduced or even absent, in cases that end in recovery eosinophilia is occasionally found. In the more chronic stages, starting usually about the third month of the disease, a small group of cases of encephalitis are accompanied by a relatively high eosinophilia (from 6 to 18.5 per cent[4] or even 24 per cent[3]). These figures are higher than would be expected if one were dealing with only the slight convalescent eosinophilia observed in recovery from acute infectious diseases.

---

1. Hassin, George B., and Diamond, I. B.: Trichinosis Encephalitis, Arch. Neurol. & Psychiat. **15**:33 (Jan.) 1926.

2. Association for Research in Nervous and Mental Diseases: Acute Epidemic Encephalitis, New York, Paul B. Hoeber, Inc., 1921, p. 91. Stern, Felix: Die epidemische Encephalitis, Berlin, Julius Springer, 1928, p. 247. Berger, W., and Untersteiner, R.: Morphologische und serologische Beobachtungen im akuten und chronischen Stadium der Encephalitis epidemica, Wien. Arch. f. inn. Med. **9**:1, 1925.

3. Berger and Untersteiner (footnote 2, third reference).

4. Stern (footnote 2, second reference).

Then again, this eosinophilia most often occurs at a time when the neutrophilic leukocytes are also increased in number; this is so unusual that it has been suggested [3] that the presence of eosinophilia plus neutrophilia may have some diagnostic significance in encephalitis.

The mechanism for the eosinophilia is not at all clear, but the mechanism for eosinophilia in other conditions is no clearer. One hypothesis has to do with the irritability of the muscles (sometimes with spasms) that is found in some cases of encephalitis. Matthisson [5] attempted to separate what she called muscular rheumatism,[6] which according to her included various forms of myositis and myalgias, from acute articular rheumatism on the basis of the eosinophilia observed in the former. She supposed that the eosinophilia of muscular rheumatism was due to the degeneration and proteolysis of the muscles involved. In support of her contention it may be remembered that a local eosinophilia is often found about degenerated muscle, as for instance in degenerated fibromyomas of the uterus. The myocardial degeneration of diphtheria may be accompanied by local eosinophilia.[7] Local myocardial eosinophilia has been reported by Hess;[8] postinfluenzal myocarditis may be associated with marked eosinophilia (Hirschfeld [9]). Even the eosinophilia of trichinosis occurs only when the parasites have become lodged in the muscle and may perhaps be related to the destruction of the latter.

Berger and Untersteiner,[2] however, found no correlation in their cases between the eosinophilia observed and the changes in muscular irritability. It is not recorded in any of the cases whether direct observation of the muscle changes was attempted. In our case there was a great deal of muscle damage with local accumulation of the cells of inflammatory exudation, among which eosinophil cells were numerous. Whether such muscle changes are more common in encephalitis than in other acute infectious diseases remains to be determined. It is significant, however, that the generalized disturbances so common in severe infections, especially high fever, were absent; the parenchymatous degeneration of acute infections, on the other hand, is most often correlated with these general disturbances. The myodegeneration that we observed may, then, be related to a specific rather than a general manifestation in this disease.

A second possible explanation for the eosinophilia in this case, and perhaps in other cases of encephalitis, is, it is true, highly speculative, but in the absence of other more definite explanations must be considered. It has to do with the possible central regulation of leukopoiesis. Schwartz [10] has suggested that the eosinophilia observed after neurotropic toxins and in disturbances of internal secre-

---

5. Matthisson, Helene: Eosinophilie bei rheumatischen Erkrankungen, Deutsche med. Wchnschr. **55**:1343, 1929.

6. Bittorf, A.: Eosinophilie des Blutes bei Muskelrhuematismus, Deutsche med. Wchnschr. **13**:354, 1919. Synwoldt, I.: Zur Eosinophilie bei Muskelrheumatismus, München. med. Wchnschr. **68**:98, 1920. Page, I. H.; Turner, R. B., and Wilson, J. H.: The Clinical Significance of Eosinophilia in a General Medical Service, J. Lab. & Clin. Med. **13**:1109, 1928.

7. Liebmann: Deutsches Arch. f. klin. Med. **117**:438, 1915.

8. Hess, L.: Zur Kenntnis der Bradycardie: Bradycardie bei eosinophiler Myocarditis, Wien. klin. Wchnschr. **32**:1131, 1919.

9. Hirschfeld, H.: Demonstration von Blut Präparaten mit ungewöhnlich starker Eosinophilie, Folia haemat. **12**:339, 1911-1912.

10. Schwartz, E.: Die Lehre von der allgemeinen und örtlichen "Eosinophilie," Ergebn. d. allg. Path. u. path. Anat. **17**:137, 1914. (This monograph contains the complete literature on eosinophilia to 1914.)

tion may be due either to a direct nervous action at the site of blood formation or to changes in chemotaxis produced by nervous stimulation acting on endocrine glands. The eosinophilia occasionally observed in other nervous diseases, chorea, epilepsy and others, may, according to him, be explained in the same way.

That the production of blood cells and the regulation of the rate at which they enter the blood stream from the sites of their origin should in some way be under the control of the nervous system, with perhaps a center comparable to the respiratory or the cardiac centers, is not at all beyond supposition, although such regulation has never been proved. As a fact, nerves to the bone marrow have never been demonstrated, and their existence is denied by some (Sabin [11]). Recently, however, there has been brought forward evidence for the existence of such central regulation. Thus, Schulhof and Matthies [12] have observed polycythemia after puncture of the brain of a rabbit in an as yet undetermined place. Rosenow [13] has found a region in the striatum, thalamus and hypothalamus, puncture of which has invariably resulted in leukocytosis. While this center is close to the center for temperature regulation, Rosenow's experiments tend to show that these two activities, temperature regulation and blood regulation, are independent of each other. Not only may the number of leukocytes be affected by disturbances of the central nervous system, however; certain evidences from human pathology, from a study of the blood in epidemic encephalitis, have pointed to a regulation of individual functions of leukopoiesis. Sato and Yoshimatsu [14] have observed that during the acute stage of epidemic encephalitis the peroxidase reaction of the myeloid leukocytes becomes negative, the oxydase reaction remaining positive, and that during convalescence the former reaction changes from negative to positive. Sato [15] has been able to reproduce this negative peroxidase reaction in rabbits by a bilateral puncture of the corpora striata, a procedure that he called the peroxidase puncture. This work has recently been confirmed.[16] When it is remembered that most of the pathologic changes in encephalitis are located in just those regions that have been suggested as centers for certain activities of leukopoiesis and leukocytic regulation, it will not be surprising that disturbances of these functions should be found in some cases of this disease. The symptomatology of encephalitis is characterized by protean manifestations; exactly what the individual patient may show depends in great part on just what part of the central nervous system is affected. So it is not to be expected that any symptoms will be constant that depend on the involvement of a small group of ganglion cells. There is, it is true, very little evidence for assuming a separate center for the regulation of the eosinophilic leukocytes;

---

11. Sabin, Florence R.: Bone Marrow, Physiol. Rev. **8**:191, 1928.

12. Schulhof, K., and Matthies, Mabel M.: Polyglobulia Induced by Cerebral Lesions, J. A. M. A. **89**:2093 (Dec. 17) 1927.

13. Rosenow, G.: Hirnstichleukocytose: Untersuchungen über die zentralvegetative Blutregulation, Ztschr. f. d. ges. exper. Med. **64**:452, 1929.

14. Sato, A., and Yoshimatsu, S.: Peroxidase Reaction in Epidemic Encephalitis: New Diagnostic and Prognostic Method, Am. J. Dis. Child. **29**:301 (March) 1925.

15. Sato, A.: Localization of a Lesion in the Brain by Differential Staining of Blood Smears, Am. J. Dis. Child. **29**:313 (March) 1925.

16. Suzuki, K.: Localization of a Lesion in the Brain by Differential Staining of Blood Smears, Tohoku J. Exper. Med. **11**:618, 1928. Shoji, K.: Experimental Production of the "Striatal Blood Picture" in the Carp by the "Peroxidase Puncture," ibid. **11**:613, 1928; The Localization of a Lesion in the Brain by Differential Staining of Blood Smears, ibid. **11**:604, 1928.

there may well be no such center. On the other hand, the regulation of blood formation by such centers may not be an immediate one, and a second set of conditions, perhaps destruction of muscle tissue, may, in a patient whose regulatory centers are disturbed, lead to unusually high eosinophilia. The solution of this problem awaits more accurate knowledge of the physiology of leukopoiesis.

It has occasionally been assumed that in cases in which a high eosinophilia has been observed, for instance the 24 per cent of Berger and Untersteiner,[2] there was a previous eosinophilic diathesis or the patient had a constitutional eosinophilia. These cases, however, were not followed long enough. In our case we considered such unusual conditions, but since the eosinophil count returned to normal values after five months, we must suppose that the eosinophilia was a temporary thing, a peculiar reaction of the patient to his disease. Naegeli [17] has denied that there is such a thing as constitutional eosinophilia or even that there is a special eosinophilic diathesis.

SUMMARY

This report concerns a case of encephalitis with marked eosinophilia (50 per cent). The eosinophilia persisted for several months, gradually declined and returned to normal within five months. The clinical picture had some resemblance to that of trichinosis, but many examinations for parasites, including several biopsies, failed to support such a diagnosis.

There are several possible explanations for eosinophilia in this case. It may have been due to the destruction of muscle tissue, which was found at the biopsies. It may have been due to a disturbance in the central regulation of hematopoiesis, with special reference to the production of eosinophilic leukocytes. This central regulation probably has its origin in the region of the basal ganglia and hypothalamus, so that pathologic changes in these regions, such as are found in encephalitis, could produce disturbances in the production of blood cells.

The evidence for the assumption of the central regulation of hematopoiesis are briefly discussed.

17. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 4, Berlin, Julius Springer, 1923, p. 158.

SPECIAL ARTICLE

ANXIETY NEUROSES

A CRITICAL REVIEW OF THE WORK OF WILHELM STEKEL*

BEN KARPMAN, M.D.
WASHINGTON, D. C.

Long before psychotherapy had come into its own as a medical specialty (and I am not sure that it is commonly regarded as such), the internist was already recognizing that certain diseases, along with the physical symptoms present, showed concomitantly a large "nervous" element. It was insisted that the physical basis was primary, while the so-called nervous component was assigned a sort of a secondary importance, perhaps a consequence of the physical. However, in spite of the application of all sorts of remedial measures, these conditions would somehow fail to respond to any physical therapy so far devised. Recent researches and clinical studies increasingly begin to support the view that purely psychic conditions are capable of producing physical symptoms that cannot be removed or cured by physical, medicinal or mechanical remedies, but only by psychic means directed at the original source of difficulties. Many visual disturbances are neurotically conditioned—the patient does not want to see the truth. The same is true of neurotic deafness—not wanting to hear. During the World War, numerous cases of hysterical deafness and dumbness were observed. Buzzing in the ear and other disturbing noises sometimes have for their purpose the hiding of disagreeable thoughts.

Of the more complex reactions one may cite reported instances of hyperthyroidism that turn out to be only physically manifesting forms of neuroses and therefore distinctly approachable by psychotherapy; of cases of cardiac, respiratory and other neuroses there is legion.

The reason why the significance of the psychic condition as a possible etiologic factor in disease has been so largely overlooked by the medical profession was probably the fact that these conditions are often, perhaps in a majority of cases, obscured by the multiplicity of physical symptoms present. Then, of course, everyone was brought

* Submitted for publication, May 7, 1931.

* Stekel, W.: Conditions of Nervous Anxiety and Their Treatment, ed. 3, translated by Rosalie Gabler, London, K. Paul, Trench, Trubner & Co., 1921; Nervöse Angstzustande und ihre Behandlung, ed. 4, Berlin, Urban & Schwarzenberg, 1924.

up on strictly scientific biologic precepts from which psychic factors appear to be eliminated. Nevertheless, modern psychotherapy is based on strictly scientific formulations.

How is it possible that a purely psychic factor should give rise to symptoms that appear to be nothing but physical and in which the original etiology cannot be discovered? It is hardly possible in the present state of knowledge to give the details of the processes involved, but something is known of the mechanism. The mechanism is explained on the principle of conversion or defense. A conversion reaction takes place when a psychic conflict is converted by the patient into an equivalent physical symptom that expresses symbolically the conflict. A person who is frustrated in love and whose "heart" is sick may transfer his emotions on the heart. Universally, it is difficult to recognize the psychic conflict present behind the physical symptoms displayed; indeed, the patient himself is not consciously aware of the meaning of his reaction. As in many other hysterical reactions, back of the whole thing is often a persistent desire to gain a particular point. One instantly brings to mind cases of hysterical paralysis in which it is learned that the patients cannot walk because they will not walk, and they will not walk because by not walking they gain certain points or advantages that they could not gain otherwise.

FEAR AND ANXIETY

Although conversion reactions may occur in all forms of neuroses, they are most frequently manifested in hysterical neuroses, more particularly in the form commonly spoken of as anxiety neuroses. The consideration of these reactions brings into view the problem of fear and anxiety.

In clinical experience, the physician meets daily with various expressions of fear. There are many patients who, when confronted with hospitalization or a medical procedure of one sort or another, show a marked fear reaction; patients have fainted from the loss of a few drops of blood and even the very sight of blood. Such fears are understandable, for behind every disease lurks the possibility of death, which evokes fear. There are, however, a number of patients who are not at all sick; in fact, they seem physically sound and are not faced with any obvious situation of danger, and yet are in constant fear. With an objective basis for such a fear lacking, the fear would appear groundless did one not realize that often the cause of fear may be concealed from consciousness and operate in a manner of which the patient is consciously not aware. One may therefore speak of fear proper as conscious fear, and anxiety as unconscious fear. However, even though the person does not consciously perceive any danger it does not mean that such danger does not exist. Indeed, it has been shown that at the

unconscious level the personality may be and often is threatened with, to it, definite danger, the reaction to which is manifested by anxiety.

Biologically, the function of fear is protection from a situation of dangerous or harmful influences; it tends to remove the person from the sphere of such harmful influences. When the danger is a consciously perceived stimulus, he may take to flight. But when he is subject to objectless feelings of fear unconsciously perceived and reacted to, the adjustment is the more difficult because it is unconscious. He really has no adequate means of meeting or escaping them and therefore remains in a constant state of anxiety.

What sort of a danger may it be that does not relate to any objective situation? From analyses of anxiety neuroses one learns that the cause or the object of the anxiety is a strong instinctive urge or craving that cannot find adequate release or outlet because of the various restrictions and inhibitions that society puts in its way. Were the man to disregard these inhibitions and yield to his primitive cravings, he would be a criminal in the full sense of the word; but when the dictates of culture are the stronger he represses the cravings in their favor. Such repression, however, is not always successful or complete. Some persons seem unable to settle the conflict one way or the other; the wish, though repressed, is still ungratified and craves expression. The personality, perceiving such frustration as a danger to it, reacts with anxiety. Then, too, although the wish is repressed and in reality ungratified, it is constantly gratified in fantasy. It is characteristic of the neurotic person, however, that he reacts to fantasy deeds as if they were truly enacted in reality. There now follows a fear of consequences and punishment, with anxiety as its emotional expression.

THE SOMATIC ASPECTS OF ANXIETY

Serious diseases need not be accompanied by any subjective complaints; nevertheless, a great many diseases are accompanied by marked feelings of anxiety. One might speak of this as secondary anxiety. On the other hand, many conditions are observed in which anxiety appears to be primary but the somatic manifestations are secondary to the anxiety. When, however, both types of reactions are studied carefully, it will be found that there is a large emotional background behind even the secondary type, and the conclusion is therefore reached that without an underlying emotional basis there is no display of anxiety; behind every anxiety is an anxiety neurosis, whether the condition is expressed by functional or by organic symptomatology.

The transformations of anxiety into physical symptoms, and more particularly the specific localization of such symptoms, appear to be conditioned on two possible factors. Generally, a person with a weakness in a particular organ—heart, chest, stomach, etc.—is more liable

to express an anxiety equivalent through that organ—palpitation, dyspnea, etc. The choice is that of locus minoris resistentiae, and the inferior organ is generally the seat of somatization. The transference from the psychic to the somatic spheres takes place more rapidly in a beaten path. People who are susceptible to a cramp in the calf are likely to experience it during an attack of anxiety. Again, the location may be specifically determined by emotional situations that require a particular organ for their expression. Thus, a cramp in a particular muscle group may be traced to the fact that this muscle group was involved in an emotional situation that is back of the anxiety reaction.

The anxiety neuroses often display a remarkable array of physical symptoms and, depending on whether the symptoms are localized in this or that organ, one speaks of the respiratory, cardiac, gastric or other form. Let it be noted, however, that although symptoms of one organ predominate, symptoms belonging to other organs are as frequently displayed. When the patient's sickness is viewed in the light of the psychic symptoms present it is discovered that the physical symptoms, for all their prominence, really occupy a rather secondary position; they have nothing in them of the permanency and fixity of organic reactions, but are rather fleeting, even elusive, and in the center of the picture stands the tremendous anxiety of the patient, an anxiety to which all other symptoms appear secondary and subservient. The basic etiology of a cardiac neurosis differs less from that of a gastric neurosis than the respective organs differ from each other. If the clinical grouping is adopted here it is mainly for purely pragmatic considerations.

THE CLINICAL ASPECTS OF ANXIETY NEUROSES

It is characteristic of the neurotic person that his instinctive life is more strongly developed, his asocial egoistic disposition perpetually endeavoring to procure enhanced pleasure for the ego. He is therefore in constant conflict with dictates of morality and culture, and in the suppression of his various asocial tendencies he has to expend so much energy that socially he becomes relatively worthless. The fear of himself and the asocial impulses drives the patient to defensive measures, among which anxiety plays a dominant part.

Patients with anxiety neuroses are a type of people dominated by their affects, and their neurosis is an expression of the disturbance of their affectivity. A life of high emotional pressure brings them more easily into conflict than normal people.

The psychic conflict explains the great irritability of patients with anxiety neuroses. Unsatisfied and unhappy, they are in a continual ferment. Their increased affectivity and sensitiveness are expressed by their touchiness and irritability. Continually preoccupied with their inner conflicts and problems, they are unable to turn their attention out-

wardly, hence their absent-mindedness and forgetfulness. Significant also are their psychic instability and quick changes of mood. They are easily aroused to fury and rage. Every useless excitement, which manifests itself in such acts as throwing and breaking things, is but a substitute for some criminal act. Often an underlying element of hate generates death wishes and becomes the source of endless self-reproaches and a tormenting sense of guilt. It is then that the affects become inhibited. Anxious expectations are thus the expression of an unfulfilled wish; the woman who fears that her husband will die is merely expressing obliquely the wish for the same, and this becomes the source of extreme feeling of guilt; hence anxiety.

Many neurotic symptoms are but punishments anticipated by the unconscious. The fear paralyzes the patients both physically and mentally. This fear and the appearance of symptoms assure the patient that the criminal act will not be committed. The arm may lose feeling because the pious man gave his hand to a strange woman, whereupon a stream of burning lust rushed through him. Many cases of paralysis have similar mechanisms—self-dictated punishments, it is true—all the more cruel for that, though executed in the name of God. The arm that would murder remains paralyzed not only to prevent it from committing the crime, but as a punishment because in fantasy the crime has been committed. A woman gives her child a box on the ears and her arm and the hand remain fixed, as by punishment of Heaven, in the position in which they were at that moment (Janet).

The apprehensiveness of the patients often takes the form of a conviction that they are suffering from mental diseases; they are threatened with serious insanity (punishment). Because these fears are unconsciously motivated and have no actual basis in fact, they cannot be dispelled by any reassurances. As to the clinical picture proper, although one is still in the dark as to the rôle of the constitutional factors in neuroses, it is becoming clear that in the creation of the clinical picture of anxiety neuroses the somatic and psychic factors work in conjunction. The following main features, as given by Freud and later elaborated by others, are to be observed in a typical anxiety reaction:[1]

General Forms.—1. General irritability, manifested by an abnormal reaction to all stimuli from within and without. The irritability is extended to all sense organs, especially to the sense of hearing, so that such an auditory hyperesthesia may arise as to cause or contribute to insomnia.

2. Anxious expectation. The patient shows an abnormal disposition to anxiety, and not on the occasion that generally produces fear and

1. All references, unless otherwise given, will be found in the original.

hesitancy. There is an exaggerated fear and anxiety over the least event or most harmless undertaking. A ride in a street-car or automobile leads to exaggerated fear for body and life; a passing pain in any part of the body brings thoughts of severe illness; the belated return of a relative calls up the worst forebodings; a noise in the house immediately suggests thieves and murderers; a business transaction of small importance leads to extreme fear of complications and disaster. The most harmless action or omission forms the starting point for moral and religious scruples which frequently become an exceedingly fruitful source of compulsive ideas, etc. While objectively the patients see the groundlessness and even ridiculousness of their fears and often try with all the energy of their rational ego to defend themselves against the compulsive nature of their fears, the efforts meet with little success.

3. Fear of death. Variable as are the phenomena of the anxiety attack, one symptom is common to all, that is, a vague torturing inexpressible fear of death. The patients localize the anxiety in various places—the heart, breast, stomach, bladder or head; some experience only a dull sense of depression. In the expressions used to convey the feeling of anxiety there is implied a certain sense of constriction.

4. Great absentmindedness and forgetfulness, the patient becoming frightened at the decrease of his mental powers. These patients fear insanity.

5. Depersonalization. There is often experienced an acute, though perhaps transitory, feeling of unreality of the ego; the patient sometimes exclaims: "I have lost myself." While orientation in time and place is correct, the surroundings lack the quality of recognition. The patients have a feeling of strangeness for their own persons as if someone else thinks, feels or acts for them. There is a disturbance in the organic consciousness; they feel the head, the arms, the hands, but as something outside the accustomed feelings of the body, or as an isolated part in strange dimensions; the head may feel empty, and the outer world has a changed aspect. These conditions are accompanied by extreme anxiety.

6. The anxiety attack. The attack may come on suddenly and unexpectedly, with great psychic disturbances, like a thunderbolt out of a clear sky, or by the gradual increase of rudimentary attacks and after certain psychic premonitions. It is sometimes preceded by irritability and slight ill humor, an expression of the sense of guilt. The patients are depressed or in a bad temper that day, although this is not the rule.

During the attack the patients feel that their end is approaching; they fear a stroke, and feel that something is entangled in their

brain; they complain of an oppressive feeling in the chest; the breathing appears to be labored. Somebody is throttling them and interferes with their breathing, just as a dying man must feel; the heart beats painfully and feels as if it would burst, or it seems to stop; they turn pale. The pulse is feeble and rapid, often arrhythmic; the limbs seem to contract, and they are unable to gain composure; the patients begin to pant and make all kinds of uneasy movements. All the symptoms that usually accompany the affect of horror or fear may also accompany an anxiety attack. The patients lose balance and must lie down. They will weep desperately—strike about them with feet and fists, the body writhing. They fight in vain for words and breath (vox faucibus haesit); the arms and legs shake as in a fever. Many patients shake violently, or experience ague (shivering fits); sweat breaks out from the whole body, the hair bristles, and the back creeps with coldness (cutis anserina); there may be cramps and paresthesia; an abnormal secretion of urine causes involuntary emptying of the bladder, or a violent disturbance of the bowels expresses itself in tenesmus, passing of wind, spasms and diarrhea; this also produces involuntary evacuation. The pupils dilate (according to Fliess, usually the left). The saliva ceases to flow, and the mouth becomes dry. Often there follow attacks of fainting, migraine, neuralgia, giddiness or tachycardia of great intensity; various pains occur in the heart, chest, stomach, and so on. During the attack the patients call for a physician, take leave of relatives and make their final arrangements. The tragic scene is often of a pronounced hysterical character.

Special Forms.—1. Anxiety equivalents. These are rudimentary anxiety attacks manifested by the usual symptoms but unaccompanied by the affects of anxiety. There is quite a scale of such rudimentary attacks, from simple discomfort and sudden depression, from an attack of sudden tiredness, up to extreme fainting and sudden collapse, thereby alarming the whole household and requiring the best efforts of the physician.

It is characteristic of anxiety neuroses that anxiety equivalents can substitute for each other. On following a succession of anxiety attacks, one has little difficulty in establishing a certain periodic sequence in some cases. The very fact that various paresthesias occur on periodic days suggests that they are an anxiety equivalent. A patient may suffer from an anxiety neurosis of a particular type, the great attacks occurring at long intervals. Then, in between the attacks, the patients may have minor attacks of a different kind; now, perhaps, trembling of the hands and numbness in the thumbs, now, violent sneezing fits which disappear shortly.

2. Phobias. These may be viewed as but special forms of anxiety neuroses in which, most often in addition to the usual manifestations,

there are particular fears directed against specific objects or situations. Thus, some patients are afraid of being in open spaces (agoraphobia), others are afraid of going through closed spaces; some are afraid of crowds; others are afraid of being alone (claustrophobia); some are afraid of getting up and going about (topophobia—anxiety of movement). Other frequent phobias are: fear of animals, fear of handling knives, fear of ghosts and the dead; railway, sea and mountain sickness (giddiness); fear of blushing and sweating; fear of examinations and fear of talking (as stammering); fear of insanity, etc. There are also many rarer forms of phobias. Not infrequently several phobias go together. Normally, human beings show fear reactions in the face of dangerous situations or because of a particular experience, and the fear is in proportion to the situation. In phobias, however, the dangerous situation does not appear to exist, and the emotional reaction is so greatly out of proportion to the stimulus or situation as to present itself immediately as pathologic.

Phobias are compromise formations. They signify a truce between dictates of conscience and the unconscious drives, enforced by the aid of anxiety. While in anxiety neuroses the fear reaction appears to be dissipated on everything in general and nothing in particular, in phobias a large portion of the anxiety appears to be absorbed by the particular object of the phobia. Away from that stimulus the person is apparently comfortable.

The reason for the fear lies outside the object of fear, for there is obviously nothing about a knife, a bridge, a bird, etc., that should induce such an exaggerated emotional reaction; in other words, phobias are merely symbols. Thus, fear of crossing a bridge may symbolize the fear of the forbidden as well as of the other shore, the hereafter; fear of tunnels may symbolize the entrance to the gates of hell which the person may fear because of criminal impulses. The railway may symbolize the devil or traveling—going into the darkness of hell and punishment. Fear of knives may be a protective device to guard one against committing a cherished but prohibited crime. Erythrophobia may be expressive of fear of being seen through—a physiologic confession of something to be ashamed of; while stammering may express a fear of betraying openly a hidden but pressing secret. The emotional reaction belonging to the original situation has been transferred to another, in itself harmless, object or idea (displacement); from the field of the unconscious it has been transferred to the field of conscious awareness, thus enabling the person to get along more comfortably; but these patients betray all that they seek to conceal. Through the aid of deep psychotherapy it is possible sometimes to unravel the meaning of the symbol, to find its equation, as it were, although admittedly phobias often show complicated psychic structures.

3. Hypochondria. In hypochondria there is a particular form of anxiety reaction in which the anxiety centers around the patient's health. Here the whole life appears to have undergone a displacement by which it tends in the direction of displeasure feelings. While each complaint in itself is not unreasonable, the totality of it strikes one as absurd. There is a tendency toward bizarre and fantastic elaboration of sensations. Hardly any organ or function of the body and mind escapes distortion, although occasionally the complaints may refer only to a particular disease and are thus in the nature of a phobia (e.g., syphilophobia). There is also a compulsive form of hypochondriasis, as in the instance of patients who say "I cannot urinate."

Although seemingly physically well, the patient will complain that his body appears to shrink until it is a "mere skeleton"; although the face seems normal, the patient will complain that the whole face is becoming distorted, the mouth and jaw are crooked, the nose is contracting and the eyes are loose and do not turn properly. The lungs do not function properly, there is a burning in the heart, the blood is either too hot or too cold, and there is something wrong with the circulation. The bowels are inflamed; there is pressure in the stomach; the arms feel as if "closed up." The urine is hot or cold, of a different color and wrong substance; the excretions are too hard or too soft. There is a continuous slight discharge of semen, etc. The patient listens to the verdict of the physician with mistrust; no one, he feels, can really understand the depth of his sickness—it is a very rare complaint; an eternal doubter, he can never be assured.

The health is thus a subject of abnormal anxiety. The least suggestion of sickness in someone else makes the patient ascribe all the symptoms to himself. The complaints thus change and shift. The patients project their anxiety on any object. They actually go in search of a disease. They adopt strict regimens of all sorts, and many of the diet cures, mountain tours, etc., are but disguised ascetic efforts. The anxiety may be dispelled by reassurance, only to have the "free floating anxiety" attach itself to another idea. Highly suggestive is the fact that the attitude toward an actually existing organic disease is one of indifference or even heedlessness.

Hypochondria is a retributive form of illness, the patients falling ill as a punishment for evil wishes, the illness taking on the very form that has been desired for another. The agitated care for his body may be a disguised care for the salvation of his soul. Correlations are often striking; here is a woman who suffers from heart trouble and whose mother died of heart failure; and there is a man who suffers from frightful pains in the small of the back and whose father died of a spinal disease. Or, to take the case of a man who alleges that he catches cold every other day: he wears two overcoats and woolen underclothing,

has his house heated on cool days in summer, and keeps it cool in winter for fear of getting overheated; he goes to bed with a thermometer. Analysis in this case elicited the fact that the man was afraid of love. He had once sustained a great disappointment and did not want to love again, although he needed a great deal of love. He did not want to feel warm again for any woman, and this idea was converted into a dread of the illness that might result if he were to get overheated and then suddenly cool down. He was perpetually reconstructing in his body the romance that had cost him his life's happiness.

Self-reproach for masturbation and the injurious effects of youthful misbehavior play an important part in the genesis of hypochondria. Masturbation is a favorite dumping-ground for every sin. It is the storehouse of the guilty conscience and is replenished from criminal, ethical and religious sources.

Indeed, the whole sex life of the patient with hypochondria shows a remarkable change. In his psyche two diametrically opposed forces are at work—sex lust and sex aversion; an overwhelming sex lust that would embrace and enjoy everything, and an all-embracing sex dread, which shrinks from every coitus as from a partial suicide. Dread of injurious consequences of coitus appears greater than sexual need; from unconscious religious motives of guilt and penance, the patients are inclined to asceticism; in hygienic considerations they seek to find a rational ground for the ascetic tendencies. However, with these patients the dread of sexuality does not mean dread of sexuality in general; the general dread only serves to conceal dread of a certain form of sexuality —homosexuality, cunnilingus, etc. Dread of syphilis or tuberculosis may take the place of dread of incest.

ANXIETY NEUROSES WITH CARDIAC PHENOMENA

Of the many organs and parts of the body on which the neurotic patient transfers his feelings of anxiety the heart is the most frequent, perhaps because in ordinary fear the heart beats faster or is in other ways perceptibly disturbed. Whoever nurtures some great sorrow, depressing obligations, an unhappy love affair or sexual disabilities is most likely to project his psychic pain to the heart.

Functional disorders of the heart may range from short palpitation, with short arrhythmia, with longer lasting tachycardia, and from an accelerated pulse rate, which often reaches a remarkable degree, to a condition of such severe weakness that the distinction from organic diseases of the heart is not easy.

While one may occasionally diagnose an organic condition as functional, the reverse is far more frequently the case. Innumerable people who go about after a diagnosis of "organic heart disease" are victims of an anxiety neurosis and a clumsy diagnosis. It is especially easy

for an inexperienced physician who is unacquainted with anxiety neuroses, when called in in a case of an anxiety attack with tachycardia, to be misled by the tremendously accelerated pulse rate, death pallor and trembling of the patient, to diagnose "vitium" and to come to the rescue with injections of ether and camphor, whereas a few comforting words and a sedative will work wonders. It is because of such hasty diagnoses that one encounters the severe, nearly incurable anxiety conditions and chronic depressions, with serious attempts at suicide. Even when the patient has a true organic condition, it is poor judgment, if not sheer cruelty, to tell the patient the true condition, for there will be superimposed then on the organic condition a severe anxiety reaction that will only make the original condition so much worse.

There are many victims of imaginary high blood pressure. An imaginary illness drives such people to seek the help of a physician. Trembling and nervous, they are already excited by the prospect that the examination will disclose some "awful illness" and their blood pressure goes up. Properly, the blood pressure of such neurotic persons should be examined while they are asleep. Patients have even been bled to control the presumed high blood pressure.

All too often the physician will tell the patient that he suffers from hardening of the arteries. The patient sees in such a diagnosis a death sentence, although one can live with sclerosed arteries for many years and can even outlive persons who do not have sclerosis. But, because it is known that arteriosclerosis may cause pain under certain circumstances, every harmless psychic pain near the heart is interpreted as a consequence of sclerosis. There are many unhappy people who die, not of arteriosclerosis, but of its diagnosis. In consequence of the diagnosis made, the poor patient promptly proceeds to change his life habits and the real torture begins. The dear modest cup, the indispensable cigar, the well spiced meals are sacrificed to cheat the threatened death by a few years or even hours. In consequence, the very opposite is often accomplished. Through sheer privation, the patient begins to wane and feels weak; this seemingly gives further support to the view that the diagnosis was correct and the illness progresses to its end. Yet sometimes the very opposite takes place. Thus, one patient complained of most acute pains, was unable to eat as before and, bowed and trembling, was hardly able to walk. A consultation of physicians was called. The patient stood trembling behind the door and listened to the learned perorations of the physicians who considered him to be in the last stages of the disease and a lost man. In a spirit of obstinancy and defiance, he rose upright and swore to himself to demonstrate to the physicians the contrary. He took up his old habits, improved greatly in every way and derided all physicians and the death over which he was now master and victor.

Some patients complain that the heart is fluttering (which symbolically means that they are fluttering or agitated); others have a feeling of vacuity, as if there is a stone in its place (the heart is empty of love); some complain of the heart vibrating (fearful expectation), while others describe a feeling as if the walls of the heart are drawn together (all love is gone). The heart is the organ that translates the otherwise difficultly understood language of the emotions into equivalent sensations. Nor is any age exempt here, for even in old age the heart does not cease to sing the melodies of love. Typical of our times are the elderly men who fear hardening of the arteries and an apoplectic fit (fear loss of love and the impotence of old age).

It need not be supposed that nervous complaints cause less aching and suffering because they are not organically conditioned. Pain is pain, whether it is psychic or organic, and if one is to believe the patients psychic pain is much more torturing and unendurable than physical pain. One may become anesthetic to physical pain, if one is sufficiently strong, but it is impossible to get away from psychic pain. How often does one hear neurotic patients offering themselves for an operation, cheerfully willing to part with an abdominal organ, with an arm or a leg to get rid of the pains and sufferings.

The most frequent form of nervous heart is certainly palpitation and accelerated pulse rate; the rate often reaches as high as 180 and more per minute; only neurotic persons can stand it. The pulse may be feeble and scarcely perceptible, the heart beats irregular and almost inaudible. The patient with a nervous heart experiences either a violent commotion in the heart, manifesting itself in palpitation, or he complains of his heart "standing still." The change of the beating from rhythmic to arrhythmic is also a common source of complaint, and is spoken of by patients as "irregularity," "flutter," "vibrations," "a sense void," "as if there is a stone in its place," "tightness," "oppression," etc. Many patients complain of violent, stabbing, unbearable pains in the heart.

Ortner is of the opinion that a paroxysmal tachycardia may lead to overstrain of the heart muscle and cause excessive pain. The cardiac pain is of a very violent, burning, oppressive, overwhelming nature. The attacks of palpitation and paroxysmal tachycardia are in most cases merely equivalents of a severe anxiety attack. Patients suffering therefrom are immensely nervous. In fact, it has been discussed whether anxiety or tachycardia is the primary trouble; clinical experience suggests that it is anxiety that is primary, but is often so disguised that it almost retires to the background. True, here and there, one encounters a case of tachycardia unaccompanied by anxiety; but it may as well be a complete anxiety equivalent. Observations made during sleep suggest that the psychic factor is a decisive one, for the very patient whose

pulse rate when awake was 120 showed a perfectly normal pulse rate during sleep.

The first stages of angina pectoris may manifest themselves by scarcely perceptible pain accompanied by extreme anxiety. Not only coronary sclerosis but also the various diseases of the heart, muscles and valves, aneurysms, pericarditis, stenosis and especially fatty degeneration of the heart may cause anxiety of a very severe nature.

The differential diagnosis between angina pectoris and a nervous heart is not always an easy matter. The symptoms of angina pectoris are well known—pain in the cardiac region, extending especially to the left arm, fear of death, sense of oppression behind the sternum, deathly cyanosis, cold sweating, enlarged pupils, trembling, vertigo, fainting, vasomotor disturbances, twitching of the muscles and convulsions. According to Ortner, hysterical angina pectoris may be distinguished from coronary angina (in common with which it may also have considerable radiation in either one or both arms, and a feeling of oppression behind the sternum and in the throat) by the particular behavior of the patient during the attack. In coronary angina the patient remains absolutely quiet. In the nervous form he cries and groans, is extremely nervous and evinces a marked tendency to move about. However, the latter symptoms are not infallibly to be regarded as psychogenic, since cases of fatal angina pectoris have been observed in which there was a marked display of emotion. A psychic superstructure over an organic disease is not uncommon. The diagnosis of an organic heart disease does not exclude a functional nervous disorder.

Along with the cardiac phenomena, there are often displayed symptoms that belong to other systems; respiratory difficulties are frequently observed. There may be difficulty in breathing, shortness of breath, convulsive respiratory movements, deep inhaling, aerophagy, pneumotosis and preinspiratory distentions of the nostrils.

ANXIETY NEUROSES WITH RESPIRATORY PHENOMENA

There is a variety of organic conditions of the lungs (as severe exudations of the pleura) and respiratory passages, as well as cases of impaired nasal breathing, that is invariably accompanied by intense anxiety, or a feeling of oppression, especially at night. Usually it is air hunger manifesting itself in the fear of suffocation; also breast anxiety. It is this very disparity between the objective disorder and the subjective state that is so characteristic of the nervous breast anxiety, nowhere so apparent as in the so-called nervous (reflex) form of asthma.

In a large number of cases, asthma appears to be merely a manifestation of a particular form of anxiety neurosis. Indeed, asthmatic attacks are often the extreme forms of lung and breast anxiety. The

anxiety is to a certain extent disguised under the mask of air hunger; or, as expressed by older authorities (Brugelman), the anxiety is the primary factor, and air hunger and various bronchial phenomena are secondary. Asthma is characterized by shortness of breath, which suddenly attacks patients who are healthy, is of short duration and sometimes, although not always, is accompanied by catarrh of the bronchioles, and then either rapidly or gradually subsides. It has also been observed that a large number of patients evince nervous symptoms. There is a sense of nervous oppression in the chest; the patients feel as if their breath is giving out, that they are suffocating, as if there is no movement in the chest; it seems to them as if other people, too, have ceased to breathe; that it is the end of the world; everybody is dying. Others describe a sense of impending suffering that hangs over them; there is a squeezing in the breast, an iron band about the chest and loins (fantasies of embrace), violent palpitations of the heart, the chest feels like a bottle that is shaken up; nausea, desire to vomit, giddiness, singing in the ears and excessive salivation complete the picture. Often, attacks occur after violent excitement or when the person is confronted by a stressful situation. Accompanying these symptoms one finds all manner of respiratory and gastro-intestinal irregularities—polypnea, cramps, tremors of the stomach. Hypnotic treatment sometimes works miracles in desperate cases of asthma.

The little known forms of asthma that can be traced to so-called womb fantasies are of great interest. There are neurotic persons who continually dwell in the fancy of being reborn. They often wake at night with shortness of breath. Their dreams mostly contain a symbolic representation of birth. (They see themselves passing through narrow chimneys; they crawl along a passage, the walls of which threaten to crush them, growing narrower and narrower, forcing the chest and head together.) The dream, which often disappears from consciousness, is succeeded by an attack of asthma. These people often show fear of narrow rooms and any kind of a crowd.

There is some material that suggests a relation between masturbation and asthma. In a case reported by Weiss, the patient was addicted to chronic masturbation. After twenty-five years of indulgence in the practice he gave it up, and this was promptly followed by a train of neurotic symptoms of which painful asthma was the most conspicuous. While the mechanism is not clear, the appearance of the phenomenon seems to be more than a coincidence.

The asthmatic attacks of these patients mostly date back to their childhood, and serve to evoke the sympathy of the family, to attract the attention of those surrounding them and to render the patients the center of universal interest. The neurotic person then responds to every humiliation and degradation with an attack of asthma, which sym-

bolically represents a flight into the past and a wish for regeneration (fantasy of a new life).

Strümpell has drawn attention to the fact that asthmatic patients manifest a psychopathic constitution and an exudative past. He points out that these patients also suffer from colica mocosa (peritoneal asthma), edema, flow of saliva, inflammation of the sinuses and intermittent pains in the joints. They were nervous already in childhood and were afflicted with urticaria, scrofula and eczema. Those interested in the question of "neurotic selection" will often realize that a neurosis makes use of the inferior organs in order to carry out its secret designs.

Many cases of persistent colds that defy all treatment are cases of anxiety neurosis, often conditioned by frustrated sexual excitement. Hay fever is likewise sometimes neurotically conditioned. Other forms of anxiety neurosis belonging to this group are hacking, barking cough, choking in the throat and irritation of the Adam's apple. In some patients one observes sudden deep sighs, the result of breathlessness, often amounting to air hunger. Glottic cramps also come within this province. Many patients lose their voices during violent emotion and sound as if they were crowing; they have a feeling as if some strange hand is strangling them. The sensation of a foreign body in the throat, a feeling as of "something sticking" in the trachea (globus hystericus), is also of psychogenic origin. Convulsive yawning, too, is a frequent symptom of an anxiety neurosis.

There exist purely psychogenic forms of bronchitis. There are people who get bronchitis at every suitable opportunity, taking refuge in disease with the aid of their bronchial muscles, which are easily irritated. A personal slight, a desire to avoid unpleasantness or a wish to reach a certain aim makes these people produce (often unconsciously) the bronchitis.

There are certain catarrhs of a most tormenting kind, in which the patient has always to clear his throat and feels a dry phlegm in it; he is generally a frequent visitor to the throat specialist, who gives temporary relief by painting the throat. In the case of many an actor or teacher (professional diseases), resistance to the unpleasantness of the vocation declares itself in the form of a chronic catarrah of the throat or the trachea, or in a temporary hoarseness that can eventually grow into a dread of catarrh. These patients tremble at every change of temperature; a falling temperature is to them a fantom of horror; they avoid smoke and dust; they cover their mouths with cloths, wear scarfs around their necks, and succumb at every suitable and unsuitable opportunity.

Breast anxiety usually manifests itself in a dull sense of oppression; the patient has a choking sensation; there is an acute dyspnea, and the patient is gasping for breath. It occurs most frequently at night. The

patient awakens out of an anxiety dream and takes a deep breath and the attack is over. Sometimes, however, the habit remains also in the day time, and the patients repeatedly have to stand still, take a deep breath, gasp and heave a sigh, after which they feel perfectly well. Most of these patients acquire the very frequent and annoying habit of swallowing air. They then have to exhale the air, as an unpleasant sensation of anxiety and oppression is produced by the distention of the stomach. Sighing is mostly a symptom of a neurosis, and all sighing neurotic patients are air consumers.

In a psychic attack of dyspnea the heart plays a large part, as the shortness of breath seems to be connected with palpitation. Short attacks of dyspnea with no objective changes in the lungs betray their psychic origin. The physiologic act that causes dyspnea and palpitation is coitus, and the anxiety dyspneic attacks suggest a sexual etiology by the exact imitation of coitus. In an attack of hysteria the resemblance is often complete, even to a correct copy of the abdominal movements. Slight night attacks of dyspnea may also be the result of a sexual fantasy.

ANXIETY NEUROSES WITH GASTRO-INTESTINAL PHENOMENA

The guilty conscience of many neurotic persons expresses itself in occult prohibitions, which sound something like this: "You don't deserve this and you don't deserve that!" As eating is one of the greatest pleasures in life, the self-dictated punishment finds easy expression in the gastro-intestinal system, which seems to be especially well adapted to the manifestation of anxiety. Over one third, perhaps even one half, of the patients with a gastric disturbance suffer from an anxiety neurosis.

Just as with the heart, organic diseases (enlargement of the heart after paroxysmal tachycardia and heart diseases after trauma) may now and then be found, so it may happen that a gastric ulcer may have a neurotic origin. One observes patients who for years have suffered from a stomach neurosis, who showed all kinds of dietetic disturbances of a hysterical nature and who died from cancer of the stomach, though only after a period of twenty or thirty years. Physicians do not yet realize that psychic forces may eventually lead to organic trouble. Delfer pointed out that nervous irritation of the organ can declare itself in an organic form and in the end actually lead to organic disease.

The association between anxiety and intestinal functions is an every day observation. Even fear felt by little children can, by sudden agitation of the organs, overcome the power of the sphincter ani. Similar things also happen to adults under the influence of fear, terror and anxiety. Various obscure cases of nervous intestinal catarrh or "nervous dyspepsia" can also be explained in the same way. Frequently, there

are even involuntary stools that escape the notice of the patient in his excitement. Intestinal diseases often begin with an ordinary cramp or diaphragm neurosis, then improve, recede and reappear, and the serious symptoms only declare themselves in the course of time.

The accompanying symptoms of anxiety as manifested by digestive disturbances are well known and express themselves most frequently by diarrhea or constipation; stomach ache; sickness; active, noisy, peristaltic movements; heartburn; choking; loss of appetite; cardialgia; bulimia, and spasms. Along with digestive disturbances one may find symptoms belonging to other organs—palpitation, perspiration, respiratory disturbances, shivering, night sweats, etc.

It is often difficult to differentiate neurotic from organic conditions of the stomach. Neurotic persons almost invariably project the stomach pains to the navel or the middle line, or else they are diffused over the whole region of the stomach, which is tender. In gastric ulcer one particular spot is always found to be extremely sensitive and tender. According to Pick, in organic diseases of the stomach, the Boas pressure point is easily verifiable on the left of the eleventh and twelfth ribs. In neurotic disorders of the stomach, great pressure sensitivity is to be found between the shoulder blades and on the spinous process itself. Nervous patients do not vomit blood, nor can occult blood be found in the stools. Roentgen examination gives negative results. If a patient whom one suspects of having an ulcer can stand solid food without any trouble and complains of pains after the taking of liquids, the diagnosis will not be difficult. The pains may not occur after eating, but they often follow excitement. The pains are not helped by hot fomentations, thermophore or morphine. The absurdity of many an anxiety idea will also betray its neurotic origin. One mostly finds that the pains are not so bad and only serve to rationalize the various idiosyncrasies.

In cases in which the patients transfer the seat of anxiety to the stomach, the attacks resemble stenocardia, but the patients localize the pain in the center of the stomach. A differential diagnosis can be made by means of theobromine sodio-salicylate or strophanthus, on the administration of which the convulsive abdominal or cardiac pains rapidly diminish, whereas if the pains are of a nervous origin relief may be obtained by the use of sedatives. It must be borne in mind, however, that certain composite forms exist in which the symptoms of the two diseases are mingled.

There are also cases of psychogenic appendicitis. Missriegler reported the case of a woman who showed fever, vomiting, accelerated pulse rate and increased sensitiveness to pressure over McBurney's point. A diagnosis was made of appendicitis. The patient refused to submit to an operation unless she was first examined by a physician who had

treated her before. On examination he observed the same conditions, but when he examined her internally she had an orgasm at the touch. Within a half hour, the fever and other symptoms disappeared. The appendicitis was a neurotic arrangement, and through unconscious cunning the patient brought about an examination by the physician.

Intestinal rumbling and atonia of the stomach are frequent symptoms of an anxiety neurosis. Two anxiety equivalents having a certain diagnostic significance may be mentioned here: vomiting and bulimia. Some patients are attacked at an unwonted hour by ravenous hunger even though they may have just had a generous meal. It is characteristic of this condition that even the immediate consumption of a substantial meal fails to satisfy the hunger. The stomach is often distended, and flatulence is frequently present. However, one must be on guard for diabetes, especially if there is polyuria and nocturia. The accompaniment of other neurotic manifestations (giddiness, fainting, sickness and perspiration, paresthesias, sleeplessness, congestion, etc.), plus the reactions of anxiety, will help in the differentiation. Sometimes bulimia may be traced to aerophagy; by taking deep breaths the patient pumps quantities of air into the stomach and causes a variety of sensations. (Air hunger is often used to produce organic symptoms: tympanism, food repeating, passing of wind, raising of the diaphragm, etc.)

These sudden attacks of bulimia, as in the case of hunger in general, have an interesting relationship to libido. A violent desire may manifest itself in the form of tormenting hunger, the hunger for love, the bulimia appearing as a sexual equivalent. The desire for life and love declares itself in a marked appetite, while loss of appetite points to the lack or the relinquishment of sexual desires.

With reference to the pathology of the inflated stomach, Jagic stated that an inflated stomach is sometimes observed as a neurotic condition, and along with such symptoms as hypersecretion, slowing of the pulse, eosinophilia, local accumulation of gases, local intestinal spasms and increased tonus of the vagus suggests a vagus neurosis (tympanismus vagotonicus). In such cases the vasomotor disturbances in the intestinal wall also hinder the absorption of gases. In these cases of tympanismus vagotonicus, the psychotherapeutist has no difficulty in observing that it is always the case of an aerophagist who in the absence of the physician is able to pump air into himself by sighing and cleverly taking breath. Hysterical tympanismus and the various appearances of swelling in the stomach are also caused by the swallowing of air. The neurotic patient can in this ingenious manner create organic substrata for his neurosis. In those who suffer from flatus and can produce flatulence by the hour, the excessive generation of gases is due to no digestive trouble, but is only a result of eating air.

"Nervous diarrhea" is also no more than a special form of an anxiety neurosis. It is characteristic of these patients that they are mostly awakened in the morning by an attack of diarrhea, which is usually traced to an anxiety dream. Even in his dreams the neurotic person is not happy. The patients have nightly erotic dreams, with fantasies picturing the prohibited and therefore accompanied by fear. Significant, too, is it that patients with nervous diarrhea can look flourishing, whereas in a true intestinal catarrh they are much run down. The neuroses grow more complicated when the patients suffer from a dread of anxiety; i. e., they fear diarrhea. The sufferer does not dare to go into society, to a theater or on a train if he is not sure of a lavatory close at hand. Flatulence also plays a great part in anxiety neuroses, as also does the fear of flatulence, which is a frequent equivalent of anxiety.

Mucous colitis appears to be a variety of nervous diarrhea and a form of anxiety neurosis. Sometimes enormous quantities of mucus are excreted with pleasurable feelings. In such cases diarrhea is the actual equivalent of an emission in which the libido is either openly manifest or operates in the form of anxiety. According to Ewald and Zweig, in cases of nervous mucous colitis no mucus can be traced in the rectum between the attacks, whereas in colitis membranacea signs of inflammatory redness and abundant phlegm are to be found objectively at all times. Foges even maintained that he found the mucous membrane in colica mucosa conspicuously pale and free from mucus during the intervals. He believed that an original functional disease like mucous colitis can develop into an organic disease, as an ulcerous colitis. He also emphasized the sexual character of the disease. These poor patients with gastric neuroses betray themselves before eating by their exceedingly characteristic behavior. Whereas the normal person enjoys and is even stimulated by the sight of food, the patient with a gastric neurosis looks suspiciously at the spread, inspects it from every quarter and asks the waiter all sorts of superfluous questions as to whether the meat is fresh and roasted properly; he looks and looks at it, smells it, carefully cuts away the margins and removes all clumps of fat; on putting the morsel into his mouth slowly and hesitatingly, he tries it again with his tongue and palate, not infrequently spitting out the first bite and putting the food aside.

On applying Pavlov's observation of the psychic basis of the secretion of gastric juice, one can readily see here how an obscure yet constantly operative fear or other underlying emotion will decidedly interfere with the proper secretion of the gastric juice with all its disturbing sequelae. Not only will digestion proper be impaired, but the stomach will be more easily susceptible to disease because of the lack of the antiseptic and bactericidal properties of gastric juice. A ravenous

appetite may sometimes be but a symbol of a strong desire, while its polar negative—disgust—may be expressed by vomiting. There is recorded the case of a clerk who was attacked by ravenous hunger only in the morning, and in spite of the distance he would have to run home for a bite. It had to be home and not a restaurant or an inn. One would suppose here that he was used to his wife's cookery. But no! The wife was never home at that time, and the little breakfast was prepared by the maid. It turned out that it was a hunger for the servant whom the man desired and loved without confessing it to himself. The desire for the girl changed into the nervous feeling of hunger, forcing the man to go home where he could meet the servant alone. A frank explanation worked wonders. The girl was discharged on some pretext, and the feeling of hunger vanished at once.

Dietetic disorders are exceedingly frequent among neurotic persons. Almost every nervous subject has his special idiosyncrasies. One cannot endure the skim of milk; a second cannot bear any kind of a fat sauce; a third retches if he has to eat raw beefsteak; a fourth can eat only liquid foods, a fifth only solids; one can eat only cold things, another only warm things; some can eat no meat; others will not touch any vegetable; some patients are afraid that what they eat will stick in their throat; others feel as if there were something sticking in their stomach; some go through a regular ceremonial at meal time; some must take a small mouthful of something every hour of the night; others are attacked by bulimia at certain hours.

With these neurotic persons the mouth is an "erogenous zone." They have mostly repressed some kind of sexual impulse (fellatio, cunnilingus, cannibalism, necrophilism). The repressed fantasy becomes associated with the act of eating, and the inhibition transfers itself from the sex act, which is morally vetoed, to the act of feeding, which then falls under the same ban.

The association between thwarted sexual excitement, loss of libido and disturbed appetite is observed in numerous instances. Many patients who complain of lack of appetite have lost sexual desire, and are either relatively impotent, because the sexual ideal is elsewhere than on the present mate, or suffer from unconscious conceptions of repugnance.

Other patients stop eating because they are everlastingly afraid of appendicitis; it might be a phobia, for the physical symptoms are lacking. The patients have dreadful pains, are very fastidious as to diet, and are very anxious in the observance of their stools. There is no better means of disturbing the normal course of the vegetative functions than by self-observation. As soon as people begin to inquire into the nature of their sleep, digestive processes and excretory functions, the sleep will assuredly be disturbed, digestion impaired and the stools

arrested. Still other patients attribute their trouble to uric acid, disease of the brain, etc. The anxiety, ascribed now a definite cause, is thus changed to fear and is therefore more tolerable.

A distinct and circumscribed form of anxiety is represented by the species of nervous disease of the stomach which preferably declares itself in hypochondriacal apprehension of a faulty diet. These patients are afraid of a faulty diet. They suffer from all kinds of disorders, such as a nasty taste in the mouth, loss of appetite, cardialgia and aerophagia. The most important thing for them is the diet, the stricter the better; but there is no kind of a diet that gives them a painless existence. They have a habit of attributing their troubles to the last food they may have eaten, with the result that the choice of dishes that suits them becomes more and more limited. In consequence of this they lose weight, grow weaker and give the impression of being ill. In looking at them, one thinks of cancer or tuberculosis, but the physical signs are negative. As they thoroughly spoil their stomachs, they are soon unable to digest heavier food; they feel an unpleasant oppression in the stomach after every meal, often put their fingers in their mouths in order to vomit, bring up a little water and phlegm, and then feel much better. Many eat little owing to a fear of pain. It is, however, to be remarked that frequently the pains felt by these patients arise from nothing but hunger; feeding these starving patients often brings remarkable results.

The most obstinate form of the species, however, are the so-called "stool hypochondriacs," who anxiously count every flatus, almost measure their daily movements, take the most expensive purgatives for constipation, which does not exist, and stop eating for fear of an accumulation of feces. The simple forms have their origin in an anxiety neurosis, just as in the diseases of the stomach. The patients begin to fear that the stools are inadequate. The apprehension arises from other sources and is transferred to the functions of the stool. Certain symbolic associations have their part in this. The painful observation of the waste products of the digestive system now commences, as also the experiments with different kinds of diet, laxatives and massage. In most cases of this kind, "spastic constipation" is diagnosed, which is wrong, for the constipation is not the result of weakness of the intestinal muscle, but rather of the excitation of the intestines.

ANXIETY NEUROSES WITH CEREBRAL PHENOMENA

There is a large number of anxiety neuroses in which the outstanding reactions cannot be attributed to the disturbances of any particular system but may be said to originate and express themselves in and through the head, in both the direct and the implied sense. One may speak of these as cerebral and group under this heading three types of phenomena.

1. *Congestion, Vertigo, Fainting.*—In the special form of anxiety known as "head anxiety," the patients complain of "congestion." All the blood, they say, goes to the head; the face burns; there is singing in the ears and a quivering before the eyes; a curtain is falling before them; their faces redden, and they have the sensation of anxiety that they are going to have a "stroke." Sometimes there may be a slight vertigo, and if the latter is associated with sickness and violent perspiration the disease resembles the Ménière syndrome. Symptoms connected with the lungs, heart, stomach or other organs are combined with it.

Vertigo may sometimes come from excessive smoking. It is often marked in some cases of food poisoning (fish, sausage or meat). Sausage poisoning especially may show such slight symptoms in the digestive regions that vertigo becomes the most conspicuous symptom and the one that causes the greatest anxiety. It may come on before the symptoms of poisoning become evident and may take much longer to disappear. In its slightest form vertigo is simply a "staggering sensation," a swiftly passing shock of the static sense. Freud described it as follows:

> The vertigo of an anxiety neurosis is neither a revolving giddiness, nor does it, like the Ménière vertigo, cause particular places and directions to stand out. It belongs to the locomotor and coordinate vertigo, like that felt with paralysis of the optic nerves; it consists of a specific discomfort accompanied by a sensation of sinking, and an impossibility to stand upright any more; the legs are as heavy as lead and tremble or else double up. This vertigo never causes a fall. On the other hand, I should like to maintain that an attack of that type of vertigo can also be substituted by an attack of profound faintness. Other conditions akin to faintness in an anxiety neurosis, can be dependent on a heart collapse. An attack of vertigo is not infrequently accompanied by the worst kind of anxiety, and is often associated with respiratory and cardiac disturbances. Vertigo at high altitudes, vertigo on mountains and abysses, is also manifested, according to observations, in an anxiety neurosis; and I do not know if it would be justifiable to acknowledge a vertigo a stomacho laeso in addition.

Vertigo, perhaps the one typical symptom of an anxiety neurosis, appears much more frequently than all other symptoms and can lead to the strangest diagnostic mistakes. Psychically, it expresses the idea: "I am not sure of myself, I cannot stand firmly, I shall fall." The fall is the "fall of man," and most patients therefore state that they are drawn toward the left side (the side of sin).

In the vertiginous attack the patient may feel weak and may feel pressure on the stomach. Patients speak of being violently giddy, as if the whole room is revolving with them; they feel as if the bed is rising and falling, and sometimes as if the head is low and the feet high. A tension in the head, as if it would burst, may precede the attack (a symbolic expression of an inability to keep back a repressed thought). They have a sensation of a veil being drawn before their eyes. There

may be a sensation of the heart ascending from the stomach to the head. The patients may have an anxiety feeling before falling asleep, as if they are about to die. The attack may also occur in the morning after a long sleep when the patient goes through a wonderfully pleasant intoxicating loss of consciousness.

To understand vertigo one must appreciate the meaning of the psychic conflicts to which the neurotic person is subject. At the unconscious level, his primitive instinctive ego craves to do certain things that are socially prohibited; at the conscious level, his moral ego (his conscience) tells him not to yield to these cravings. Vertigo then arises from the fear that the instinctive ego might overpower the moral ego.

The difference between vertigo and faintness is this: With vertigo the conquest threatens, but the conscious mind regains the mastery after a few seconds of struggle, whereas with faintness, the mastery slips from powerless hands, the instinctive wish being fulfilled in a dream.

2. *Insomnia.*—Insomnia is among the frequent and disturbing symptoms of an anxiety neurosis. Uniformly (as an overvalued idea) or in rapid succession (almost like a flight of ideas) thoughts occur through the mind at night, when the patient with anxiety neurosis is withdrawn from the distractions of the day. The general anxiety is increased by the terrors of the night. All the accumulated anxiety clamors for release; the night is in a measure reserved for prohibited and especially for sexual thoughts. It is at night that the "secret criminal" makes his appearance.

It is not difficult to diagnose insomnia that occurs as the result of an anxiety affect. The patients are seized with the feeling of anxiety before falling asleep, which they generally attribute to some organic cause. They are afraid of something happening, that they will be seized with a stroke, that they are on the verge of a severe illness, that their heart will cease to beat; "This must be the end; that is how one feels when about to die." The anxiety thoughts chase one another in riotous confusion, or else only one thought—sometimes an isolated meaningless word—roves monotonously through the field of consciousness.

The study of these isolated words, which are only apparently meaningless, is interesting. A lady who felt impelled to hum a melody for hours at a stretch and could not sleep sang a melody that was a familiar song: "I am a widow, a little widow," etc. Concealed behind this harmless song were death wishes against her husband. It most frequently happens that those suffering from an anxiety neurosis fall asleep and are then awakened by an anxiety dream. The familiar sensation of falling from a height and the sudden fall in which the whole body makes a convulsive movement are sensations generally occurring in the first stages of sleep, and are frequent symptoms in patients with anxiety neuroses.

The sleep of the patient with anxiety neurosis is generally restless, full of wild, confused dreams, out of which he awakes with a throbbing heart and bathed in perspiration; he is unable to fall asleep again for a long time. The dreams that trouble him are often of a typically erotic nature. Women dream of men who pierce them through the breast; of great savage men who pursue them; of gigantic steers who follow them; of neighing stallions, etc. Men dream that they are in a position of great danger; that they have failed to pass an examination; that they are standing as prisoners at the bar. Here and there, incest dreams or perverse impulses (homosexual dreams) frighten the moral ego and compel consciousness to reassume its control. But the dreams betray still more. The neurotic person dreams of murder, of corpses, of criminals. When once one has mastered the language of dreams and gained insight into them, one is amazed to find what a severe contest the patient with an anxiety neurosis is engaged in against his criminal impulses. All anxiety is fear of oneself. The criminal thoughts come forth at night and demand realization. They want to be more than mere fantoms. It is then that the neurotic person becomes afraid of himself. He sees before him the yawning abyss of his soul. Perhaps he cannot sleep because he fears the evil thoughts in his dreams.

As long as a neurosis persists, sleep can hardly be induced. Drugs usually fail, or unusually large doses are required. Bromide is the most effective soporific as it reduces the libido and the cerebral excitement. It is amazing how quickly the insomnia of some neurotic persons vanishes when their excitement is allayed by sexual gratification (if it is normal). There is always a certain amount of anxiety dissipated by the sex act, but which, if accumulated, makes people ill (for example, women whose husbands are away).

A most frequent cause of insomnia is abstinence from masturbation in cases in which the patients struggle to break themselves from the habit. In place of pleasure, anxiety appears as its equivalent. After an act of masturbation they are able to sleep peacefully. For some people, masturbation is the only effective soporific. In the place of abandoned masturbation there is often an increase of nocturnal emissions; but all emissions are merely onanistic acts with the elimination of consciousness.

Insomnia also frequently occurs after an operation. This insomnia was regarded for a time as being the result of fear, anxiety and the toxic effect of chloroform. This is only partly true. The anesthetic and the operation are a severe psychic trauma for the sexual fantasy of the patient. One needs only imagine what it means to a modest woman to lie naked before a number of men and allow herself to be operated on. It is such a complete break with everything that has hitherto been modestly preserved that the fantasy must be greatly excited. Dreams after an operation prove that the operation is the point of issue for

violation and prostitution fantasies. Nocturnal fits and screaming may be regarded as extensions into adult life of pavor nocturnus.

Anxiety dreams may precede a severe infectious disease (typhoid). It is not in any sense a prophetic dream, but merely that with disturbed metabolism, conscious thinking is lessened and a freer sway is given to fantasy life.

3. *Nausea, Vomiting and Related Phenomena.*—Choking, hiccups, retching and even chronic sickness can also be symptoms of an anxiety neurosis. The cases of so-called "nervous sickness" are cases of repressed fantasies linked with the affect of disgust. The sensations of disgust are transmitted in a very roundabout way into a tendency to vomit and into actual sickness. The thought of things that are repulsive to people only produces a feeling of nausea if a sensation is combined with this thought; aversion is then the fear of contact, and vomiting is a most acute defensive reaction of the organism to overcome this.

The feeling of nausea appears to be acquired and not inborn, and bears a relation to the development of the sense of shame. Perhaps originally it is likely to have been a feeling of surprise and strangeness that certainly bore a resemblance to repulsion, since most persons find every new, unaccustomed article of food more or less distasteful and can only bring themselves to partake of it after a certain amount of initial resistance has been overcome.

A search among a number of people for objects that arouse aversion will nearly always bring to light certain sex symbols. On the other hand, repugnance can also be toward the unaccustomed and more particularly to that which is associated with certain unpleasant conceptions (conditioned reaction). Many persons find kidneys repugnant because they think that the urine washes over them; others can repress or neutralize disgust. Again, habit may generate disgust; a dish partaken of many times becomes repugnant. Disgust thus has a certain regulating biologic value in that it drives the organism, always hungry for stimulation, to seek new reactions.

Cases of cardialgia accompanied by feelings of aversion occur frequently with an anxiety neurosis. Sometimes considerable difficulties may arise, especially when the actual anxiety feelings are absent and vomiting appears as an anxiety equivalent. Whenever, in the psychic conflict, the sexual aversion carries a higher value than the opposing sex impulse, there is a "nervous" sickness. The psychic conflict may relate to sexual disharmonies, violent repressions and unconscious ideas of disgust. The poison complex often plays a part, as do sometimes the attempts to ward off coprophilic and cannibalistic impulses.

Especially in women, if the anxiety neurosis is accompanied by sickness, it strongly suggests an emotionally colored sexual repudiation, that is, disgust. Such patients are frequently frigid.

The food idiosyncrasies, which are often psychically conditioned, are very significant. There also exists a "psychic anaphylaxis." The sensitiveness of the patients against certain foods grows to such a pitch that grave organic symptoms make their appearance, which almost suggest a toxemia. There are, for instance, people who cannot bear the skim of milk and have to vomit if they chance to swallow some. Other neurotic patients cannot eat blood food, raw beefsteaks, black puddings, etc., and are obliged to vomit if they eat only a mouthful of them (repressed sadism, vampirism). In many cases an apprehension of the results of having eaten certain foods is formed. Even the thought of food causes certain defensive reactions of nausea. Frequently they are only superficial associations with the blood complex—carrots, all red foods, red fruits, etc. Other conceptions of anxiety belong to the province of phobias, fear that they might swallow small animals, fear of poisonous food, the poison complex, etc. The central point in all these symptoms, then, is the fear of injurious results, a secondary expression of the fear of punishment of a guilty conscience.

Because of marked repression, woman's attitude toward sex is largely tinged with anxiety and disgust, which must be overcome by the power of instinct. The stronger the feeling of displeasure, the greater will be the woman's resistance to the sexual act. If pregnancy results, and if for one reason or another it is not desired, the wish may arise in the woman's soul that her resistance at the time had been greater. The succeeding acts of vomiting may then be conceived as forming the psychic substitute for the great aversion that failed before coition. This appears to be the most probable mechanism behind hyperemesis gravidarum. There is the instance of a woman who, having conceived, not by her husband but by a lover, was so tormented by the sickness that an artificial abortion was considered, whereas, in the second pregnancy there was an entire absence of vomiting, the mechanism apparently being that bad conscience, self-reproach and perhaps even the feeling of disgust for her own offense had been transmuted into the physical act of vomiting. Nervous women, therefore, tend much more to vomit in this condition than those with strong nerves and a robust conscience. Here, as elsewhere, the two factors must work together in order to bring about the disease; the physical factor (toxemia) and the psychic conflict. Perhaps many of the other disorders of pregnancy may be explained in this way. The morbid cravings of pregnant women may also be psychically conditioned.

The sickness of pregnant women manifests an unconscious setting of hate for the new-born child. This element can persist after birth. In most cases the hatred is transformed into exaggerated love (exaggerated reaction formation). It is the women who harbor hostile feelings for the child during pregnancy who become exaggeratedly fond mothers.

Even the ordinary menstrual disturbances are often conditioned by nervous influences; every physician knows of instances of amenorrhea when it is feared because the patient has had a good reason to fear pregnancy. In the case of high school girls the upsetting fear of the examinations is likely to bring about amenorrhea.

Pregnancy is universally regarded as a disease of nine months' duration, and there is little doubt that pregnancy facilitates the development of a severe anxiety neurosis; indeed, some of its phenomena correspond strikingly to the symptoms of the anxiety neurosis. The best known symptom is a change of taste as regards food. Many persons evidence such disgust for meat that they cannot swallow a mouthful (symbolic expression of sexual rejection). Others have peculiar cravings that recall the desires of hysteric and chlorotic patients. A tendency to fainting, palpitation, asthma, diarrhea, constipation, salivation, spasms and fits of shivering completes the picture. The mingling of hope and fear as to the outcome, which is felt to be uncertain, may play a large part in the development of the neurotic reactions. The anxiety that is naturally connected with birth is transformed into an objective fear, and the pregnant woman becomes filled with bad forebodings. They are depressed and cry; they know for sure that they are going to die, and it is noteworthy that a large percentage of all female suicidal attempts is made during either menstruation or pregnancy. The sickness of pregnant women becomes more comprehensible when one reflects that there are many women who are obliged to vomit after every coitus with their husbands.

ANXIETY NEUROSES WITH VEGETATIVE AUTONOMIC PHENOMENA

Symptoms referring to the vegetative autonomic (including endocrinologic) systems proper are frequently, one would say universally, present in anxiety neuroses and give rise to the strangest subjective and objective phenomena. The symptoms already described as belonging to one or another system could with equal justice be spoken of as belonging to or as being a function of the vegetative autonomic system. Hence, even when the latter is more or less directly involved, the symptomatology does not lend itself easily to distinct classification, which at best must be accepted as more or less arbitrary. For instance, cramps, pains and other disturbances in the bladder, prostate, urethra and vaginal muscles that sometimes accompany anxiety neuroses can with equal profit be classified under the disturbances of the genito-urinary tract as under the vegetative autonomic disorders. In a tentative way, therefore, one may describe them under the following headings.

1. *Sensorimotor Phenomena.*—The patient with an anxiety neurosis is frequently subject to a variety of sensorimotor disturbances, of which paresthesia, in its many forms, is the most frequent. The patient may

experience a "crawling" feeling on the face or other part of the body, often of a burning character. The skin feels greatly irritated, as if the body were continually charged with electricity. Here and there one observes, as an accompaniment, acute pains.

Along with paresthesia, one must also consider "coldness and numbness of the limbs." Probably "acroparesthesia" also has some intimate connection with anxiety neuroses. Cases of pruritus paresthesia are not infrequently observed in anxiety neuroses. Paresthesia may sometimes be so troublesome as to give rise to insomnia.

The case is recorded of a woman, who was suffering from "collapse" of the heart. During an attack she had a complete deadening of the fingers on the right hand, while the skin and the nails became blue and cold. The feeling spread through the entire body as if everything became numbed. In an analysis of the case it was found that she was playing death by the partial mortification of her limbs, while her fear of the heart collapsing was symbolic of a conflict between the death wish and the life impulse.

Cases of pruritus vulvae with induced scratching are occasionally encountered. The pruritus ceases with a slightly pleasurable feeling that has a tranquilizing effect on the woman's previously excited nerves, and she finds that she is then able to go to sleep. These may be regarded as disguised forms of masturbation. Indeed, Stekel believes that it is the urge for masturbation that originally stimulated the handling of the genital parts which, on prolonged abuse, leads to pruritus. Sheuer reported such a case occurring after masturbation. Cases of pruritus ani may have similar mechanisms. Such an inversion of symptoms is not unusual in hysteria.

2. *Neuromotor Phenomena.*—In the neuromotor manifestations of anxiety neuroses, trembling and shivering are perhaps the most conspicuous. These patients will complain of the trembling of the hand or the shaking of the leg, or the whole body may be involved. The latter may take the form of periodic attacks of ague. Fits of shivering are not uncommon.

There are patients who have a great variety of pains. One patient cited by Janet showed at the age of 17 many respiratory symptoms—feeling of suffocation and pain in the breast. This was followed by pain in the gullet so that she could hardly swallow. At the age of 21, the pains moved to the stomach—digestive pains, vomiting, etc. At 23, the seat of the pain was the uterus, with an enormous discharge of fluid that resembled a nasal hydrorrhea and was unlike a metritis. At 30, the pain had extended to the back and then to the head, and finally established itself in the face. The pains in the various organs were identical, which suggests that the alleged pain was not in this or that organ but was psychic and an expression of general anxiety.

Muscular cramp frequently accompanies anxiety attacks. The patients complain of various disorders: The hand becomes stiff; a leg contracts convulsively; there is a pain in the shoulder, an unpleasant cramp in the calves, dorsal pains of various kinds, cramp and cramplike conditions in the muscles under the control of the sympathetic system—heart, stomach, intestines and bladder. These reactions are the result of stimulation by the affect of fear and anxiety, the initial response being characterized by excitement, while with more severe conditions the effect is expressed by paralysis of the muscles. A timid person screams, but a frightened person loses his voice. Many of these cramps are resistance movements and protective measures subserving some unconscious idea. These muscular cramps are indications of anxious excitement; i. e., the action of the sympathetic muscles may be excited and that of the voluntary muscles inhibited.

Many movements of the head and cramps often embody a particular representation. The woman who constantly makes a negative sign with her head merely signifies a negation of the act of infidelity when she said "yes," to her subsequent regret. The memory of the experience is now forgotten (repressed) and she is now continually saying "no." It is as if she were trying to protect herself against a fresh temptation by saying "no" in advance. It is a frequent symptom of subsequent correction. These muscular phenomena really come under the category of "tics."

Muscular cramps were frequently observed among soldiers. Self-deception was as common among officers as among the rank and file. The muscular cramps that are known as occupational neuroses may similarly have a psychic origin. Sometimes, preceding the onset of the neurosis, there may develop in the patient a deep-rooted antipathy for his occupation.

Another form of occupational neurosis, which shows in a like manner the power of unconscious resistance, is the remarkable laryngeal cramp, which is particularly liable to affect singers who do not love their profession. They fear public appearance and would rather be supported by parents or for various reasons do not care to continue in it.

Besides muscular cramps, muscular pains play a certain part in anxiety neuroses. Freud, in his work on anxiety neuroses, pointed out that many so-called rheumatic pains are only symptoms of a disguised anxiety neurosis. The same might be said—even with greater justification—of the "gouty" pains once so fashionable—gouty neuralgia, etc. Such uric pains are often miraculously cured by medical baths. But that is only because the women are removed from the injurious effects of coitus interruptus and form new connections here and there in the health resorts, and because the men satisfied their desire even if out of wedlock. These enigmatic "rheumatic or gouty" pains arise, as in the

case of the paresthesias, through a form of conversion, i. e., by the transformation of psychic into somatic phenomena.

If a patient suffers from a cramp in the esophagus, in the absence of any organic etiology, it is suggestive that he probably does not want to eat because he is tired of life. If the food sticks to the throat and the patient has continuous difficulties in swallowing, a malignant neoplasm or esophageal diverticulum may be considered; but if the condition remains stationary for one or more years, roentgenograms are normal and the probe passes without difficulty, an organic cause may well be eliminated and a psychogenic background be considered—perhaps an unconscious homosexual fellatio fantasy, as some cases show. Sometimes it is the inability to swallow certain types of food. In the category of rare cases of anxiety rudiments are also included convulsive contractions of the gullet (with or without singultus) and cramp of the esophagus.

The so-called cardiac pains that young people complain of are, in the majority of cases, psychic pains that have become projected on the heart as the seat of all emotions. In older people who suffer from arteriosclerosis, a differential diagnosis is more difficult to arrive at.

Abdominal pains are not infrequently of neurotic origin. Cases of pseudocholelithiasis have been observed, while cases of "false appendicitis" are numerous. Fear of appendicitis may induce a similar condition. When the abdominal cramp is mistaken for appendicitis, the pain may be very severe and the peristalsis remarkably increased. An examination will reveal great sensitiveness in McBurney's region, but the pressure sensitiveness, it will be observed, is confined to the skin only. If the skin is pinched the patient will cry out, but intensive and deeper pressure, if imperceptibly increased, occasions no pain. The pains thus appear as anxiety equivalents of a purely psychogenic nature; appendicitis is nonexistent.

A rare symptom of anxiety neurosis are the perineal cramps. This symptom, together with nervous tenesmus, urge to urinate, irritation in the vagina, pains in the testes, irritation in the urethra and coccygodynia, belongs to those rudiments of anxiety neuroses which are rare and difficult to detect. These cramps often end with a fairly intense feeling of pleasure. A physician thus described his attacks of perineal cramp, "I often suffered as a child from diarrhea. I had a bad attack of this malady when I was 6 years old, complicated by severe tenesmus. This tenesmus remained with me and occurs from time to time without any special cause. I feel a strong impulse to defecate, but am unable to do so. A violent contraction in the rectum causes such pain that I could cry out. This pain gradually resolves itself into a pleasurable sensation, which ends in an actual orgasm. Sometimes the cramp occurs only in the perineal region."

This case is interesting because it introduces a characteristic disorder of the bladder. The patient suffered, among other things, from such a violent polyuria that he was obliged to urinate every ten minutes. This symptom is common and is indicative of a sexual excitement and the transference of anxiety to the genital tract. In this case there was also intense pain in the urethra, which increased during urination, and then too resolved itself into a feeling of pleasure.

Disturbances in the bladder in the form of cramp in this region are also well known to urologists. Gonorrhea particularly may greatly complicate anxiety neuroses and delay their cure. Sometimes gonorrhea brings to light some latent anxiety neurosis. These patients often suffer from dreadful cramp in the bladder, and at the same time produce a perfectly clear second urine.

The prostate may also be the seat of neurotic phenomena. The prostate feels to the patient like a stone or a foreign body. The sensitiveness of the organ increases during walking and may reach such a pitch that the patients are unable to sit down (akathisia). These attacks drive the patients to distraction. The cramp may pass from the bladder, then to the anus and then to the prostate, or vice versa. It is generally due to repressed homosexual tendencies. This would account for Pryors' case of a man getting cramp of the prostate while watching copulating dogs.

The function of urination is especially subject to anxiety neurosis. The first symptom of an anxiety neurosis is often a frequent desire to urinate, which is sometimes so imperative that the patient is liable to wet himself as he can never reach a lavatory in time. These patients develop a phobia; they are afraid that this weakness may attack them in public, and they therefore shun society, never going to a theater, because the very thought of urination produces a desire to urinate, and they eventually suffer from dread of society. Many patients are troubled with fear that they cannot urinate, that they may become incapable of urinating, and functional paralysis of the detrusor vesicae is the result.

Vaginism often occurs in young married women whose husbands are inexperienced, relatively impotent or maladroit. The women become irritable, tearful and apprehensive and complain of palpitation, vertigo, fainting attacks, migraine, etc. It is well known that an anxiety neurosis is very liable to break out in young married women if they are still anesthetic; i. e., if the sexual aversion is not yet overcome. Vaginism, too, may be due to psychic causes. If a woman exhibits vaginism with her husband but shows none of it with a friend, the cause, like that of anesthesia, must be psychic. In reality, the vaginism has the same psychic motivations as nervous vomiting, abdominal cramp, food idiosyncrasies, etc., and expresses disgust or resistance against the sexual act or the partner.

In the anxiety neuroses with neuromotor phenomena, in addition to the general picture of the anxiety reaction, one finds universally intrusion of symptoms belonging to or coming from other symptoms and organs. There may be oppression in the head, migraine, fainting, vertigo, palpitation, emaciation, dyspepsia, constipation and profuse perspiration; the arm may be weak or numb, as if dead, and cannot be moved.

3. *Vasomotor and Constitutional Phenomena.*—As a group, patients with anxiety neuroses are peculiarly liable to disturbances in the vasomotor system. Flatau observed two groups of diseases in which associations between anxiety and vasomotor disturbances were in evidence: (1) urticaria and swelling of the joints in women; (2) pathologic blushing and a feeling of impediment of speech (stammering, stuttering, etc.). The chief cause of blushing (erythrophobia) is secret onanism accompanied by forbidden fantasies. The anxiety over it may be recognized by the eye furrow, paleness, sunken cheeks, flabby expression of the face, etc. The blushing is often masked by all sorts of devices (deep hats, growing a large beard, etc.). There is also an anxiety over growing pale. These neurotic persons grow pale at social events, and the reaction finally makes them absolutely asocial. Sometimes blushing and growing pale change places.

But patients with anxiety neuroses are also otherwise disposed to vasomotor phenomena, and their vasomotor lability is the cause of countless paresthesias. They nearly all evince distinct symptoms of dermographism; they easily change color, sometimes turning pale, sometimes dark. In some, excitement will produce urticaria. Excessive perspiration (if this may be added to the vasomotor phenomena) is an exceedingly frequent phenomenon.

Constitutional disturbances are also frequently observed in anxiety neuroses. Of these, fever is perhaps the best known. Edema of the feet may be an accompaniment of an anxiety neurosis and may be psychically determined. Gutheil reported a case of Quincke's edema, psychically determined and cured by psychoanalysis. Freud reported the case of a man who suffered from agoraphobia and who after crossing a road exhibited extreme, extensive edema in both legs. However, if his family physician accompanied him, the man could walk for three hours without a feeling of anxiety and without a trace of edema. Swelling, too, may similarly be observed in anxiety neuroses, as in the case of a woman who suffered from an anxiety neurosis with cerebral and cardiac manifestations. Later on, she had a feeling before the attacks as if her feet were swollen; this was no hallucination—the soles of the feet were actually swollen. This premonitory swelling of the soles of the feet, which occurred with her also as an anxiety equivalent, had its particular explanation. Her husband was accustomed to tickle her—she was extremely ticklish—with his big toe on the soles of her feet when

he desired to stimulate her erotically. This symptom was also the prelude to the anxiety attack. The peripheral nerves were so highly sensitive to excitement that a temporary transudation was caused (angioneurotic edema).

Hartenberg drew particular attention to the interesting phenomenon of "periodic emaciation." There are patients in whom, when having an attack of neurosis, a much run-down physical condition and a marked loss of weight develop along with other symptoms. Physical examination fails to reveal a somatic basis for this condition. This periodic emaciation is never a primary symptom. It occurs only as a result of stubborn anorexia, which in turn owes its origin to secret disgust. Loss of appetite and aversion are nevertheless sometimes denied, so that the conspicuously rapid emaciation can scarcely be accounted for. On studying such a case, however, one has no difficulty in finding other symptoms of anxiety, and then the rapid loss of flesh appears merely as an incipient anxiety neurosis. Along with periodic emaciation one occasionally observes periodic obesity, especially in states of depression (compensation for loss of love).

ANXIETY REACTIONS IN CHILDREN

Pavor nocturnus is the infantile form of anxiety neurosis, and its clinical picture is characteristic. Strong no less than nervous children sometimes fear darkness and being alone, for they miss the person of whom they are fond, but are calmed if the person holds their hand in the dark. In nervous children, however, it is often observed that suddenly and without any special reason a certain irritability and a kind of exaggerated anxiousness appear; although accustomed to being happy in the dark, they suddenly refuse to remain alone or to enter any room that is dark. In an attack the child jumps up in bed, very often uncovers itself, screams, in many cases talks confusedly and seems to be absolutely unconscious, behaving like a somnambulist. Other children during the attack see fire, glowing balls, large knives, huge animals, black men, robbers, etc.

Along with anxiety reactions proper, there are often absentmindedness, enuresis, eczema, attacks of diarrhea, vomiting, slight fainting spells and occasionally decidedly phobic reactions. Sometimes pavor nocturnus is merely anticipatory of developing epilepsy, for in addition the children may have fainting spells (petit mal?) and symptoms like flickering before the eyes (aura?).

In spite of its apparent multiformity, the etiology of anxiety neurosis in children may be summed up under two main headings: (1) general psychic factors referable to intrafamilial relations, and (2) sexuality in an open or implicit form. In actual practice it is difficult to separate the two as they often commingle, so that cause and effect are not easily

discernible. Contrary to the opinion held by the majority of pediatricians who look for a physical etiology of the conditions, pavor nocturnus and related conditions are not caused by constipation, cold in the head, overloading of the stomach, improper feeding, infection of adenoids, etc., since these conditions are present in other children who are free from pavor. Hence, such remedial measures as a spacious bedroom, a hard bed that is not too warm, the avoidance of excitement, attention to the regularity of stools, the passing of water before going to bed, etc., are only of secondary importance. Pediatricians often state that the condition is sometimes due to a disturbance in the central nervous system, but the statement is vague and merely substitutes one unknown factor in the equation for another. As it has been observed that children of nervous parents are especially liable to the illness, the conclusion has been drawn that pavor nocturnus is expressive of an hereditary tendency. This statement, however, contains only half the truth; the observation is correct, but the explanation is wrong. Children born of nervous parents are nervous not so much because they have inherited the nervousness from their parents but because nervous parents create a home environment that is surcharged with "nervousness." The father and mother may not get along; one or the other or both may suffer from a neurosis with all its attendant display of symptoms. Should the wife be dissatisfied in marriage, her unsatisfied love life will express itself in great irritability toward her husband and compensatorily in an exaggerated love for the child, who serves to satisfy all the needs for tenderness. Such love often goes to the extreme (excessive petting and kissing, sleeping in the same bed, even physical manipulation, etc.) and awakens prematurely the erotic instincts of the child, with all the devastating influences of such unnatural attitude on its psyche, leading eventually to the development of a typical neurotic child. It is here that infantile sexual trauma often originates. The severe psychic conflicts of incest fantasies, compulsion neurosis, conversion hysteria, etc., in adult neurotic persons are often traceable to this sort of infantile experience.

An obscure erotic emotion expresses itself in a child in a feeling of anxiety. Therefore, children could sometimes easily be cured of those fits of anxiety if they were taken away from the bedroom of their parents and put to sleep in separate rooms. Children often overhear incidents of married life when the parents think that they are fast asleep and can hear nothing. Unfortunately, one still imagines a child as a nonsexual being. Children must never sleep in their parents' bedroom. Harmful influences come not only through parents. Other people of the opposite sex can under certain circumstances exert on the child a sexual influence of which the child is not aware, but which is strong enough to release an anxiety affect from the unconscious.

One cannot be too cautious in dealing with children. This applies also to children of the same sex. A sexual impression on a boy from his father or from a tutor may be of great importance in building up a permanent homosexuality.

In the analysis of adult neurotic persons, scenes of sexual attacks frequently emerge from memory; sexual traumas are not infrequent as etiologic factors in neuroses, although children seldom tell of these attacks. Aberrant sex conduct, even seduction by elder teachers, nurses, et al., can play a considerable part in the dynamics of neuroses. It is true that such traumas are also found in the history of people with a sound nervous system; not all children react with neuroses to such traumas. Very often the trauma maintains its special meaning only through the neurotic setting of the patient. True, too, is it that many forms of neuroses develop without a psychic trauma. Whether in a given setting the child will or will not develop a neurosis depends to a large extent on the particular psychic disposition and on the inhibitions that the child receives from his surroundings. That is why children of parents of comparatively little culture bear traumas relatively without damage, while children living in a highly cultured milieu with its religious and ethical inhibitions often become strongly neurotic.

The thoughless behavior of elders toward children and exaggerated fondness, especially kissing on erogenous zones (mouth, neck, even anus, etc.), stir up the erotic instincts of the child and lead to masturbation and to the establishment of other perversive behavior. The sexual excitement is often frustrated and leads to the development of anxiety reactions. This applies especially to "only children," who seldom avoid great damage done by exaggerated tenderness.

Many cases of children's hysteria with convulsions and delirious fits show, during the attacks, erotic imitations; many cases of pavor nocturnus can be cured at once if the child is removed from the bedroom of its parents or is taken away from a pretty and tender-hearted governess.

Large emotional factors may often be found in the nervousness of children—humiliation, neglect and unfair punishment—leading to suppressed rage and a consequent anxiety attack. Children's jealousy is often of an unsuspected strength. Jealousy is, perhaps, the basic phenomenon around which other symptoms group themselves. The child is not only jealous of one parent but of both. It vacillates in its love between father and mother, and would like to keep each parent for itself. This jealousy must be neutralized and made harmless. Especially is this the case in unhappy marriages; for the child takes sides very early; this attitude contributes toward the building up of a neurosis.

Children, it must be remembered, are little savages with all their primitive instincts. Fundamentally selfish, the child wishes the death of every person who gets in its way. However, a child looks on death, not in the adult sense, but merely as a means of getting rid of someone, a sort of temporary removal or disappearance; the child does not have the same fear of death that adults do. Hence, death wishes by children are not originally accompanied by the same degree of emotion. Behind children's ideas of getting rid of someone there is often an emotional motive; more particularly, jealousy of parents and other siblings. Children often imagine that other brothers and sisters are loved more than they are themselves and thus often wish the death of their rivals. With the awakening of conscience, which occurs early, they come to fear the consequences of a bad conscience; they are afraid of punishment by God, who sees and knows everything. The talion law corresponds to the naive primitive thinking of the child. If he wishes something, even death, to a little sister or brother, and if that one dies, then some signs of anxiety neurosis or compulsion neurosis may soon be noticed. The anxiety of the child may therefore be conditioned on sexuality, criminality or both. Death, especially, plays a prominent rôle in the anxiety dreams of children; "death trauma" is frequent. It is good pedagogics to protect children from strong impressions; gruesome fairy tales should be avoided. What is needed in the education of children is not fear, but wisely balanced love that will avoid neurotic excitement and yet give it the tenderness that it cannot do without. On the other hand, lack of tenderness makes children as neurotic as excess of love. If a child develops an anxiety neurosis, there is no doubt that an educational mistake has been made.

Anxiety reactions are sometimes significantly observed in children coincidentally with their unwillingness to attend school. Now and then one sees cases of a "school or teacher" phobia developing. Certain teachers become the object of neurotic anxiety. Children are seized with anxiety when the teacher looks at them; their whole body shakes, and they can never give a proper answer. These are mostly cases of erotic settings. The children are in love with the teacher (male or female) and often convert this love into hatred, as they believe they do not get enough attention. They suspect slights and imagine that the teacher has a dislike for them; in short, they have an emotional attitude toward him. Often, changing the school is the only measure that saves the children from "teacher phobia." In a few cases a quick cure by using analytic, pedagogic methods may be obtained.

Suicide among children often follows in the wake of an anxiety neurosis; sometimes, perhaps, as a personal retribution for death wishes: "No one kills himself who would not have killed another." Suicide in childhood sometimes shows connection with giving up mas-

turbation. The child cannot bring the severe conflicts between impulse and morality to an issue and so flees from life. Often, suicide is intended to be a deep (eternal) punishment to the educators for their supposed lack of love. Again, frequently, it is jealousy that leads a child into an insoluble conflict.

ETIOLOGY, DIAGNOSIS, PROGNOSIS AND TREATMENT

Since Beard first separated the concept of "neurasthenia," the latter has become a sort of diagnostic waste basket into which all sorts of clinical conditions were indiscriminately thrown. In 1893, S. Freud, in a careful clinical study of the problem, separated from neurasthenia two conditions:

1. Actual (somatic) neuroses, having in their etiology chemical intoxication with toxic substances consequent on some actual abuse of the sexual functions and without the assistance of psychic factors. The constitutional element was presumed to be large and the condition not approachable through psychotherapy. Within this group are found three types: (1) Anxiety neuroses: These occur whenever the sexual libido is separated from its psychic goal (frustrated sexual stimulation: coitus interruptus, etc.), which is subjectively felt as anxiety. Its main symptoms are: general irritability, anxious expectation, anxiety attacks with somatic, vasomotor and secretory disturbances. (2) Neurasthenia: The causative factor is masturbation which, when excessive, results in psychic exhaustion. Its main symptoms are: pressure in the head, spinal irritations, constipation, paresthesias, diminished potency and depression. (3) Hypochondria: Demonstrable changes in the organs are lacking and generally have never been present.

2. Psychoneuroses. In these only psychic factors operate. They include: (1) Hysteria: The etiology is traced to psychic traumas, repression, etc. (2) Obsessional neuroses: Certain ideas force themselves unmotivated into consciousness. There is a compulsion to repeat coordinated but purposeless and senseless movements.

In 1908, Stekel went further in the delimitation of these clinical conditions and asserted that every morbid fear was psychically determined and curable by psychic means; there was therefore no justification for separating actual neuroses from psychoneuroses, all being psychoneuroses. He maintained that no physical harm ever came to the nervous system because of frustrated sexual stimulation, but that the latter may prove to be a contributory factor if there is, to begin with, an underlying neurosis; lacking such a conflict, sexual frustration per se cannot produce a neurosis. The basis of such a conflict is often the inability of the person to find a form of sexual satisfaction adequate to himself; or there is a severe conflict between criminality

and morality, for an anxiety neurosis is a disease of bad conscience which might arise from tabooed and social impulses. Stekel did not deny the influence of somatic factors, but believed that somatic and psychic factors work in conjunction to produce the clinical picture of anxiety neuroses. He believed that endocrine glands play a large rôle, and that under the influence of toxins inhibitions are removed and suppressed tendencies are released, creating conflicts.

To meet Stekel's objections, Freud proposed to distinguish two sorts of anxiety neuroses: (1) anxiety neurosis (true) with a somatic basis; (2) anxiety hysteria, with a psychic basis, presenting the familiar mechanisms of hysteria.

Originally Stekel accepted the compromise, but he now uses anxiety neurosis, not in Freud's sense, but purely as a psychoneurosis. The many cases cited in his book support considerably his contention.

As etiologic factors in anxiety neuroses one finds, therefore, on superficial observation anyway but rather prominently, frustrated sex life, such as enforced abstinence, coitus interruptus, incomplete gratification of one sort or another, a loveless marriage, etc. However, on deeper analysis, one finds intense jealousy and revenge with wide ramifications into incestuous, auto-erotic, homosexual, sadomasochistic and other paraphiliac drives. On this basis there arises a sense of guilt and anxiety over retributive punishment. The etiology may sometimes turn out to be very complicated, especially if there is an admixture of compulsive features. Besides the influence of sexual life as a cause of neuroses—sufficiently emphasized by freudians—Stekel's work also shows the importance of ambition, conflicts between criminality and morality, religious feelings and the instinct of self-preservation.

The diagnosis of violent anxiety attacks is mostly gained from the lips of the patients, their facial expression and certain objective symptoms which, although typical, have nothing like the constancy of a law. The picture must be judged as a whole and not by its individual symptoms.

The manner in which the patients receive the physician is characteristic. The physician is met with some such words as, "Help me, I am so terribly afraid; I am dying, this must be the last hour." There may be violent screaming and speechlessness. The legs totter, the hands tremble, the hair stands on end. They give free expression to a variety of somatic complaints, usually centering about one or more organs. Frequently, they complain of dryness in the mouth and throat, great thirst and ravenous appetite. However, cases with excessive salivation have been observed. The face is pale, and the eyes bulge out of the head because the lids are open to the utmost, proclaiming the fear of death. However, the face may be very red (probably a combination of anxiety and anger). A cold sweat breaks out on the

forehead. The pupils dilate; according to Fleiss, the left pupil dilates to the utmost before the attack—a valuable premonitory symptom.

Urinary urgency, small quantities of grape sugar (M. Kaufmann), diarrhea and even involuntary stools occur in extreme cases. Circulatory disturbances are often prominent. The pulse is rapid and small. According to S. Kornfeld, there are a rise in the blood pressure and an alternation of the pulse curve, which consists in a diminution of the rising limb of the pulse wave that synchronizes with the systole of the left ventricle. Acute dilatation of the heart has been observed in the acute condition.

The subjective complaint of anxiety is not always expressed or evidenced. Sometimes, the patient will complain of various symptoms without directly complaining of anxiety, or there may be just frightful excitement and torturing unrest. Finally, the anxiety may be thrown into the background, and the symptoms displayed are anxiety equivalents.

The duration of an anxiety attack varies within wide limits: from a few minutes sometimes to hours.

Characteristic are anxiety dreams in which there is much dreaming of death. Relatives appear who are already long dead; one sees living persons in coffins, or one attends a funeral procession. Next to death dreams, dreams of rape predominate in anxiety dreams. Robbers and thieves appear and throttle the victim; knives, revolvers, sabers, cross-bows, fire, water, narrow ravines and sudden falls play a great rôle; also wild animals, bulls, stallions and raging, biting dogs. Criminal thoughts of poisoning, arson, etc., express themselves in characteristic anxiety dreams.

The differential diagnosis must be made on the one hand from a number of physical and organic conditions, and, on the other, from other neuroses and psychoses. Anxiety neuroses must be differentiated from physical and organic conditions because these are often accompanied by anxiety reactions and may have an anxiety neurosis superimposed on them. Certain acute (as atropine, hyoscin, cocaine, amidopyrine, sulphonethylmethane, etc.) and chronic (as nicotine, alcohol, morphine, cocaine) intoxications are often accompanied by marked and sometimes violent anxiety; more frequently as abstinence phenomena. The differentiation from other physical conditions (heart, lungs, etc.) has already been given in the respective accounts.

The early stages of some infectious diseases, as lyssa and typhoid fever, often begin with sensations of anxiety, and anxiety dreams are commonly found in them. The effect of psychic suggestion can be excluded in these cases as the patients do not know the nature or danger of the condition.

Exophthalmic goiter shows a number of nervous phenomena that may occur in anxiety neuroses, viz: dizziness, headache, increased sensitiveness, restlessness, insomnia, constant trembling, palpitation and sweating. In a number of cases of anxiety neuroses one often finds a greater or lesser struma. Many "formes frustes" of exophthalmic goiter are nothing but anxiety neuroses manifesting themselves through the thyroid apparatus.

From diabetes, anxiety neurosis must be differentiated because the complaint of dryness in the mouth or throat, great thirst and ravenous appetite and pruritus are common to both.

Neurotic anxiety must be carefully differentiated from general nervousness, which is not conditioned by any neurosis. This fearfulness has always a corresponding psychic motive based on an actual situation. But the distinction is not always practicable, seeing that cases of general nervousness increase to attacks of anxiety, and behind such a nervousness there may sometimes be discovered distinct neurotic mechanisms. In the case of neurotic fear, the disproportion between the object of the fear and the discomfort leads to the diagnosis, even if other signs are absent.

The differentiation of anxiety neuroses from psychoses with anxiety features is not difficult in typical and well developed cases. In such cases one finds, in addition to an anxiety reaction, other features that specifically belong to psychoses. Thus, in acute hebephrenia one finds additionally delusional and hallucinatory reactions, while in melancholia there are tormenting self-reproaches and self-accusatory delusions. Too, the sense of guilt in psychoses is much more pervading and consuming, hence the great frequency of suicide, whereas the patient with an anxiety neurosis only makes gestures in that direction. In the early stages of psychoses differentiation is difficult and requires a careful study of the personality. Intellectual disturbances are invariably present in psychoses, whereas in neuroses intelligence remains intact and at most only secondarily affected. Emotional disturbances in neurotic patients are largely quantitative exaggerations of the normal; in psychotic persons one finds qualitative changes, that is, emotional deterioration. In every psychosis there is a profound transformation of the personality; in neuroses, the personality remains intact. While the neurotic patient is afraid that his body will fall to pieces (punishment for sexual digressions, etc.) and shows an emotional reaction appropriate to the expressed fear, the psychotic patient, under like circumstances, is convinced that his body has already fallen to pieces, expressing his belief with the utmost indifference. While the megalomanic ideas of the neurotic patient (Messiah and martyr complex) are obviously compensatory wish fulfilments, the grandiose delusions of the psychotic patient express deep convictions. These and many other

differential features reveal that in neuroses and psychoses one is dealing with two fundamentally different types of reactions, expressive of widely different types of personalities. One must, therefore, guard himself against the mistake commonly made that a neurosis may pass into a psychosis if it reaches a severe enough degree. Neuroses never pass into psychoses, or vice versa.

The differentiation of anxiety neuroses from other neuroses should not be difficult if a careful personality study is made. The homosexually conditioned neuroses (overt homosexuality, sadomasochism, fetishism, etc.) may present anxiety features, but these are not prominent, while the paraphiliac reactions stand in the foreground. In obsessional and compulsive neuroses one observes frequently attacks of panic with a large element of anxiety in them, but in these, in addition to anxiety, there are to be found other emotional reactions with states of doubt, indecision, etc.

In the estimation of the prognosis, one has to be equivocal; although anxiety neuroses are reputed to be easy of treatment, the cure must be pronounced with reservation. It must not be forgotten that the patient with an anxiety neurosis is the first cousin of the hysteric patient with an anxiety neurosis is the first cousin of the hysterical And in the hysterical patient one must bear in mind the personality and the symptoms. Admittedly, the latter may be relieved, but it is doubtful, at least in the present state of knowledge, whether one can as completely reconstruct the hysterical personality. Furthermore, the relief from the symptoms is not always the blessing sought; sometimes the disappearance of the physical symptoms is followed or substituted by certain behavior reactions, essentially antisocial in character, and one sometimes wonders whether society is not better off when the patient himself suffers with somatic symptoms than when he makes people around him suffer through his vicarious behavior.

As for treatment, it seems that nothing less than thorough-going psychotherapy will do the work effectively; even this sometimes fails. Unfortunately, these patients often go through the hands of many physicians—internists, specialists of one sort or another (depending on the most outstanding complaint), and neurologists—before they ever reach the office of the psychotherapeutist, by which time they often appear in a most deplorable condition. Countless are the neurotic patients who have been fed and overfed on all sorts of diets and drugs by the gastro-enterologist, or digitalis by the heart specialist, etc., until they actually develop the physical trouble for which they are ostensibly treated. The lay medical practitioner still looks on psychic conditions as being only imaginary and feels himself thoroughly competent to treat such conditions. Even the neurologist (certainly the great majority of them), whose training should have taught him better, still

regards the treatment for functional nervous disorders as his legitimate field, although his knowledge of psychotherapy is ever so small, his understanding of the practice being practically synonymous with the use of simple suggestion, assurance and fatherly advice, which, after all, is "common sense psychology and good salesmanship," to quote one of them. Let no one, however, beguile himself with fancies that these patients can ever be cured by such simple methods; that because these patients are very suggestible, suggestion will cure the condition. Babinski's fantasm still follows us like Banquo's ghost. Because it is convenient, physicians still cling to his idea of hysteria as a condition that can be produced by suggestion and cured by persuasion. This concept has limited understanding of the neuroses and has done much to retard the progress of psychotherapy. Daily experience teaches that hysterical conditions as they are found clinically are not produced by suggestion, and the number of hysterical conditions that can be so produced is infinitely small as compared with the number that are not so produced; one hears but little of cures by suggestion.

To tell the patient that his symptoms are only imaginary is, of course, absurd. Is not the patient right when he retorts, "Why don't *you* imagine something, doctor?" Even if the symptoms have no established organic basis, they nevertheless, have a basis; while they are intangible to us, they are very real to the patient. This is why the effect of suggestion is short lived. After a few treatments the patient may admit that he is entirely well and the neurologist prides himself on having accomplished a brilliant cure. He may never see the patient again, not, however, because the patient is cured, but because as the effect of suggestion has worn off and the symptoms have returned the patient harks now to the office of the next neurologist who, too, using suggestion, accomplishes another brilliant cure. And so it goes.

In the nature of things suggestion cannot be effective because it is primarily static and not dynamic, dealing with the symptoms as such and not with the genesis and evolution of symptoms or their psychologic significance; it aims to effect a change in the patient's life by the mere removal of the troublesome manifestations and not by a psychologic reconstruction of the patient's emotional life. In so doing, it effects a change of conduct, often very temporary, and not a psychologic cure, leaving the patient to react at the same low psychobiologic level at which the conflicts arose.

There is much more to suggestion than mere assurance or admonition; it has behind it a complicated psychology of its own and it may sometimes be used successfully, provided the physician understands well the psychic mechanisms involved. There is also much more to psychotherapy than suggestion. It is essentially the treatment for any condition, physical or psychic, by psychic means, and in a large sense,

therefore, it encompasses the whole field of medicine. As a medical speciality it requires fully as much, and, in the opinion of some authorities, even more, preparation than any other branch of medicine. Whether one prefers to limit his psychotherapeutic approach to psychoanalysis in any of its forms, to the system of Janet, Adolph Meyer or other methods, one must above all be fairly conversant with the entire field. Hence, one who has not trained himself to do this type of work is treating the patient under false pretenses. It is unfair to the patient and therefore unethical because it misleads the patient, giving him a false sense of security. One needs only to go through the cases cited by Stekel—and admittedly many of them are superficial —to realize the therapeutic problems with which the physician is confronted when attempting to treat patients with neuroses.

In all, the treatment for neuroses, of which anxiety neurosis is but one outstanding instance, must be left entirely in the hands of that medical specialty which has for its immediate province the understanding and treatment of abnormal mental and emotional states. The surgeon who operates on a fantom tumor, the internist who feeds the patient on all sorts of medicines, fancy diets and exercises, the neurologist who uses suggestion and the urologist who treats psychic impotence by the introduction of sounds, massage of the prostate, or what not, are all either consciously or unwittingly guilty of malpractice, for they are treating the patients for a condition the meaning of which they do not understand. Considering that a large portion of the practice is functional, it is singularly true that no distinct contributions to psychotherapy have come from the internist or the neurologist, and when such contributions were made, as in the instance of Charcot, it was when he left organic neurology for the functional field. Psychotherapy is still a sort of a step-child of medicine. It is in the best interest of the practice of medicine, the physician and the patient as well, that psychotherapy should be given its own right, for only then will it be able to contribute its full share in the treatment for psychic diseases.

1720 Irving Street, N. W.

News and Comment

TWELFTH ANNUAL MEETING OF THE ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The twelfth annual meeting of the Association for Research in Nervous and Mental Disease will be held on Monday and Tuesday, Dec. 28 and 29, 1931. The headquarters of the Association will be as usual at the Hotel Commodore, Forty-Second Street and Lexington Avenue, New York City, and the sessions will be held in the rooms that have been engaged by the Association in the past. The meeting will consist of morning and afternoon sessions, the former being called to order promptly at 9 a. m., and the latter at 2 p. m.

The 1931 program will be devoted to consideration of "Infections of the Central Nervous System." The program will consist of the following papers:

First Day: Morning Session

Symposium on Poliomyelitis and Epidemic Encephalitis:

1. Biologic Reactions in Poliomyelitis, Epidemic Encephalitis, Postinfectious Encephalitis, Postvaccinal Encephalitis. Dr. Joseph H. Globus, New York.

2. Filtrable Viruses in Infections of the Central Nervous System. Dr. Thomas M. Rivers, New York.

3. Pathways of Infection to the Central Nervous System: *a.* Anatomic Approach to the Central Nervous System by Blood and Lymph. Dr. David Orr, Edinburgh, Scotland. *b.* Clinical Aspects. Dr. Foster Kennedy, New York.

4. The Poliomyelitis Problem from the Point of View of Its Epidemiology. Dr. W. Lloyd Aycock, Boston.

5. Critical Résumé of the Treatment of the Acute Stage of Poliomyelitis. Dr. Lewis J. Pollock, Chicago.

6. Summary and Critique, and Work Done by the Milbank International Committee on Poliomyelitis. Dr. William H. Park, New York.

Afternoon Session

7. Etiology of Epidemic Encephalitis. (*a*) Dr. Frederick P. Gay, New York. (*b*) Dr. Earl B. McKinley, Washington, D. C. (*c*) Dr. Edward C. Rosenow, Rochester, Minn.

8. Encephalomyelitis. Dr. Israel Strauss, New York.

9. Treatment: Review of the Work of the Matheson Commission. Dr. Josephine B. Neal and Dr. Inez A. Bentley, New York.

10. Summary and Critique. Dr. Hans Zinsser, Boston.

Second Day: Morning Session

Symposium on Meningitis:

1. Pathology. Dr. George B. Hassin, Chicago.

2. Bacteriology. Dr. Anna Williams and Ruth Gosling, New York.

3. Epidemiology. Dr. George McCoy, Washington, D. C.

4. Types of Meningeal Reactions, Including Bacterial and Aseptic Meningitis and Meningismus: Incidence and Differential Diagnosis. Dr. Frank Fremont Smith, Boston.

5. Bacterial Meningitis. Dr. Josephine B. Neal, Dr. Henry W. Jackson and Dr. Emanuel Appelbaum, New York.

6. Meningococcus Meningitis. Dr. John E. Gordon, Detroit.

Afternoon Session

7. Meningitis in Infants. Dr. Roger Dennett, New York.

8. Antimeningitis Serum. Dr. Benjamin White and Dr. Elliott S. Robinson, Jamaica Plain, Mass.

9. Surgical Treatment in Meningitis. Dr. Walter Dandy, Baltimore.

10. Meningitis: Experimental and Therapeutic. Dr. John A. Kolmer, Philadelphia.

11. Summary and Critique. Dr. Josephine B. Neal, New York.

Thomas K. Davis, M.D., *Secretary.*

THE CHICAGO ACADEMY OF CRIMINOLOGY

The Chicago Academy of Criminology, which was organized last spring, has for its main purpose the establishment of a common meeting ground for all who are interested in the scientific study of the criminal and the prevention of and treatment for crime and allied behavior problems. Monthly meetings will be held for the discussion of these topics, and should lead to better understanding and cooperation among workers in the many different aspects of this field. The membership includes psychiatrists, psychologists, social workers, jurists, educators, pathologists, toxicologists, experts in crime detection and police and prison administrators. At the first regular meeting on May 14, 1931, the following officers were elected: president, Edwin H. Sutherland, Ph.D., professor of sociology, University of Chicago; vice presidents, Dr. Ludvig Hektoen, director of the John McCormick Institute for Infectious Diseases, Dr. Paul L. Schroeder, criminologist to the Illinois State Department of Public Welfare, and Arthur J. Todd, Ph.D., professor of sociology, Northwestern University; secretary and treasurer, Dr. Meyer Solomon, of the Northwestern University Medical School.

At the second meeting, held on June 4, 1931, Clifford R. Shaw, head of the department of research sociology of the Institute for Juvenile Research and Behavior Research Fund, presented a paper on "Delinquency Areas in Urban Communities." The third meeting was held on October 8, with the following program: (1) Historical Development of the Prison System in the United States, by Edwin H. Sutherland, president of the Academy; (2) Modern European Prison Systems, by Harry M. Fisher, chief justice of the Criminal Court of Cook County, and (3) Modern Prison Program of Illinois, by Rodney H. Brandon, director of the State Department of Public Welfare.

FIRST INTERNATIONAL NEUROLOGICAL CONGRESS, BERNE, 1931

The Transactions of the International Neurological Congress will not be published in full. A small volume, however, will appear containing the following: (1) the officers of the Congress; (2) the honorary members; (3) the permanent committee of organization; (4) the program committee; (5) the speeches of welcome; (6) the conferring of honorary degrees; (7) the program of the sessions, with the abstract of each contribution presented before the Congress and the discussion that followed, together with a notation indicating in which journal the contribution is to be published in full; (8) the minutes of the executive session; (9) the speeches in full and the resolutions presented before the Congress at the final evening conference on September 4; (10) the program of entertain-

ment for the active and affiliated members; (11) an alphabetical list of speakers; (12) a list of the active members with their addresses; (13) a list of the affiliated members, and (14) the list of contributions that could not be presented. This volume will be ready in a few months, and will be sent, postage prepaid, to all who prescribe on the receipt of 10 (Swiss) francs. Subscriptions should be sent to Dr. Charles Dubois, Secretary, Falkenhöheweg 20, Berne, Switzerland.

Many of the original papers read at the Congress will be published in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. Abstracts of the four principal symposia will also appear in this journal. The October, 1931, issue of the *Revue neurologique* is especially devoted to the International Neurological Congress, and contains an abstract of its entire proceedings. Copies may be obtained at the price of 30 francs (French) from Masson et Cie, 120 Boulevard Saint-Germain, Paris, VI, France.

AMERICAN PSYCHOANALYTICAL FOUNDATION

The American Psychoanalytical Foundation has been established with the object of fostering psychoanalytic education and science in America. It is incorporated in the State of New York and succeeds the Educational Trust Fund formed by the New York Psychoanalytical Society several years ago.

Obituary

AUGUST FOREL

1848–1931

With August Forel's death a most active and effective career has come to a close. I may be pardoned, I hope, if I give a rather personal account of this remarkable man. In the early eighties, the name of Forel had become familiar even among us youngsters at the Zürich gymnasium through the interest aroused by his work with hypnosis; and, in 1887, evidently in my third medical semester, when curiosity led me to browse among the current medical publications, I noticed in the *Archiv für Psychiatrie und Nervenkrankheiten* of January, 1887, his "Hirnanatomische Betrachtungen und Ergebnisse," and was captivated by the outlook offered. I attended at that time the first or the second course in brain anatomy that von Monakow gave, a course with many illustrations of the experimental methods of von Gudden. H. H. Donaldson had brought the Golgi results to Zürich, and Forel combined the data of the Golgi method with the wealth of experience of the Gudden school and thereby laid the foundation for the neuron theory by experimentation, at the same time that His did it by embryologic research.

As a teacher of psychiatry, Forel was too nondogmatic to create a distinctive school, but, as with his views on the hypnosis problem, he remained on a sound common-sense basis, monistic, somewhat neurologizing, but after all always tolerant of the consideration of what the patient did and said. Forel made himself strongly felt, moreover, by his fervent appeals for total abstinence from alcohol and by his share in legislation abolishing the licensing of houses of prostitution. His appearance at a large "Commers," one of the huge beer feasts of the entire student body, with the courage to propose a toast with and for a nonalcoholic beverage, proved to pass without his being hooted down, and established the respect even of his critics. With the greatest intrepidity, he was ever frank and direct in meeting his opponents in the civic and in the faculty ranks. He was a character always aboveboard.

Stimulated by Gowers' account of the anatomy of the spinal cord, in 1890, I decided to obtain the same accuracy and clearness in the more complex parts of the nervous system and to prepare my thesis on a topic of cerebral anatomy, and I applied to Forel for a problem. Here again, in my first more personal contact, I met the man of tempera-

ment. Had I not known his manner, I should have retired before the bald refusal to bother with candidates who would probably start on something and then force him to finish the job. I let him storm for ten or fifteen minutes and was finally led to the laboratory and a collection of sections and, owing to the presence of a series of sections stained by Delbrueck, to a problem of the independent eye movement of the chameleon. I had to stand my ground in the matter of the choice of methods and the change to the study of the forebrain. I had to find my own way. Forel came to the laboratory but once or twice to finish his contribution to the Kölliker Festschrift (the experimental demonstration of the origins of the nerves of the posterior hindbrain segment), and incidentally, to scold me for using Weigert's "Bierfilz" method. But to be able to study his anatomic papers with the sections on which they were based made up for the temperamental one-sidedness of the critic. When I brought him the finished thesis, we became good friends and remained so, notwithstanding the fact that I never became a militant total abstainer, as Forel would have liked. Yet he respected my independence.

As a medical student or young graduate, Forel had won a prize with his classic work on the "Ants of Switzerland." In 1872, he did his thesis work with Theodor Meynert on the optic thalamus. In 1873, he became assistant of von Gudden in Munich and continued his brain studies, bringing great clearness into the anatomy of the brain stem. At the same time, he laid the foundation of his clinical and practical psychiatric training. In 1879, when Hitzig left Zürich, Forel, but 31 years old, received the Zürich post, which he held for nineteen years. A fighter, but perfectly square and honest, he had his enemies, and, tired of the arduous task and troubled somewhat with gout, at 50 he retired to an independent life in his old home at Chigny near Lausanne. There, and later at Yvorne, he devoted himself to his life interests and to his family—his remarkably sympathetic and capable wife and their five children. From time to time he went on expeditions to study the ants of many regions (in his early life he had gone as far as the West Indies, where his companion, the father of the young woman who became his life companion, succumbed to a fever). With a limited practice, Forel carried on his world-wide work on the alcohol problem and maintained social, political and ethical and philosophic-monistic contacts and interests. In 1899, his affiliation with the Good Templar Order brought him to Toronto, and at the same time he received an invitation to attend the decennial celebration of Clark University, where he spoke on hypnosis and on the habits of ants. It was at this celebration that Ramón y Cajal gave his lectures on the cerebral cortex and Mosso his lectures on the visceral participations in emotions —a most memorable occasion. Wherever Forel went, he left a deep

impression. A cerebral thrombosis damaged his speech and deprived him of the use of the right hand in 1912; but even after that he would attend congresses and extend his personal influence in a remarkable manner.

With the most exacting scientific discipline so well exemplified in his work on ants and in his studies on the brain, Forel combined the courage to attack large human problems with fervor and a remarkable ability to achieve practical results. Uncompromising, with quick wit, and a French slant and clearness even in his Swiss German dialect and German lectures and writings, he wrote and spoke with unusual directness and incisiveness, always true to his outspoken convictions. He was in close contact with the socialist leaders of many countries; he was a militant pacifist (sit venia verbo), an exponent and defender of ethical progress, a man of untiring action, respected equally by friends and by those whom he felt he had to attack. Those who learned to know his son at the Mental Hygiene Congress in Washington got a sense of the type of ardent temperament and fairness that will ever go with the name of August Forel.

ADOLF MEYER, M.D.

Abstracts from Current Literature

BINOCULAR VISION AND PROJECTION. ALEXANDER DUANE, Arch. Ophth. **5**:734 (May) 1931.

This is the second of two posthumous articles published through the courtesy of the widow of Dr. Duane. The first, appeared in the *Archives of Ophthalmology* (**5**:1 [Jan.] 1931) and considered in detail "Accommodation." The second continues that specialty within a specialty (which was the outstanding characteristic in all of Dr. Duane's writings on extra-ocular muscles). In all but a small minority of cases, binocular fixation is present whenever one looks with both eyes. The image of the object looked at, then, is formed on each fovea. In spite of this, though there are two images, one sees not two objects but one object, which differs notably from the impression derived from each eye when seeing separately. This, as the author states, illustrates binocular single vision. Fusion is the phenomenon that has occurred allowing the sensory impression received from the two foveas to be fused into a single sensory impression. How this occurs is not known. It seems well established that the neuron in the occipital cortex with which each member of such a pair of foveas is connected is close to the neuron that is connected with its fellow, and that the two neurons thus constituting the cerebral representatives of each pair of corresponding points habitually work together to produce a common mental impression. Whether they do this with each other or by communicating with a common center, known as the fusion center, is undetermined.

The factor of corresponding retinal points in the fusion of images is of greatest importance. (Corresponding points are two points on the retinas that are equally far away and have the same direction from the fovea in each eye.) This has already been referred to.

In discussing the horopter as a circle passing through the object of fixation and the nodal points of the two eyes, Dr. Duane has shown how corresponding points will lie in the retina if the eyes do not undergo torsion. In convergence, as is known, however, the eyes undergo torsion while converging, so that the two points on which the retinal images of one object fall, and which would be correspondent in the two eyes if the vertical meridians had remained vertical, no longer correspond. This hypothesis is worked out on the basis of torsion in convergence, but it is concluded by Duane that this element does not affect the horopter for ordinary ranges of vision.

Fusion of dissimilar objects, i. e., stereopsis, and the degree of its perfection in the normal size is discussed. This applies especially to the two foveal images, and constitutes the conception of differing impressions and their conversion into a single visual concept which combines the character of the two, affording at the same time a sense of solidity and an impression of depth lacking in the monocular picture.

The second part of the paper continues with binocular projection. In monocular projection there are both visual and postural elements. The visual element helps one to localize an object through the impression that this retinal image produces. The postural element has two factors; the first is present in monocular and in binocular projection; it is the sensations derived from the movements of the head and from the conjugate movements of the eyes that make one aware that the latter are directed right or left, up or down, and that thus tell one how objects are situated in a transverse plane; the second factor is sensations that are derived from movements of convergence. These sensations are the distinguishing feature of binocular projection, differentiating it thus from monocular projection and serving to explain all of the phenomena of binocular diplopia. The net results of these two distinctive factors of binocular projection, i. e., fusion, or the visual element, and convergence, or the postural element, result in a visual concept that

lies in a midline between the two eyes as a more or less definite point on that line, but which appears single. It is as if the single image, or binocular projection, was performed by a single cyclopean eye situated in the midline between the two eyes, with its visual axis directed along the midline, with its fovea representing the combined foveas of the two eyes and with a point representing the combined nodal points of the two eyes. Such a point may be called the binodal point, and the visual line representing the fusion of the two visual lines of the two eyes may be called the bivisual line. This bivisual line can be directed ahead, sideways or up or down, but its direction will always be given by a line connecting the binodal point with the object of fixation.

This projection by the binoculus, or binocular single vision, is performed just as it would be by each eye if each eye were transferred to the root of the nose and then rotated, the left eye to the left and the right eye to the right until the fovea of each was in the midline. In the explanation of binocular single vision, the five intrinsic factors in estimating distance are included because of their interest: (1) differences in accommodative effort; the nearer object demands more accommodation than the farther; (2) mathematical perspective; one object is judged nearer than the other because of the size of the retinal image, i. e., the nearer object has the larger image; (3) dissimilarity in the retinal images of the object fixed, i. e., the left eye sees the front and left side of an object, and the right eye sees the front and right side of it; (4) differences in the muscular effort of converging, i. e., the nearer object demands greater convergence than the farther, and (5) physiologic double images; objects closer than the one fixed appear with a crossed diplopia, and objects beyond that fixed appear with a homonymous diplopia, i. e., their images fall on noncorresponding points.

A drawing illustrating the projection from the binoculus, modeled in part after LeConte and included in the text elucidates these five factors well. By studying this drawing the explanation of binocular single vision is made clear; it is as well definitely stated. The binoculus is simply the representative of the linked pairs of visual centers in the cerebral cortex and the representative of the combined retinas of both eyes. The projection is made with reference to the midline, instead of with reference to the right or the left visual axis as it is in monocular vision.

In connection with data which Duane had already given in the article, projection with relation to the visual plane is next presented. For example, if sensations coming from the muscles of the head tell one that the face is directed straight forward, and at the same time the sensations derived from the muscles of the eyes assure one that the elevators are in equilibrium with the depressors, it is known that the visual plane is horizontal and that the object of fixation is neither above nor below. The movements of the eyes are strictly associated, so that when an impulse is sent to the elevators in one eye an equal impulse is sent to the elevators in the other eye; this is also true of the depressors. It follows, therefore, that projection with relation to the visual plane relates objects situated on the right and the left to the bivisual line, or those above or below to the visual plane.

Projection by the binoculus as an explanation of physiologic diplopia is then considered in detail. This, as already stated, is one of the points in the estimation of distance.

The law of binocular projection, developed as a result of the observations on the binoculus, may be stated as follows: When the two eyes act together, each contributes a visual impression that is first transferred to the midline and then projected, as it would be in monocular vision. In other words, in binocular vision, projection by each eye is made as if each had been transferred to the midline and had remained motionless, i. e., neither converging nor making a conjugate movement—projection as if guided by its visual impressions alone. Two component impressions that have a like origin in the two eyes will therefore be seen as double. This statement applies not only to physiologic but to pathologic diplopia.

The essential differences between monocular and binocular projection, it is thus seen, are that in the former each eye projects as if it were in its own place, and in the latter as if it were transferred to the midline. In monocular vision each eye projects with reference to its own visual axis; in binocular vision, with reference to the midline or bivisual line.

The sighting or dominant eye in binocular projection is discussed in detail. Duane in considering this gives but little credit to the dominance of an eye—of right-eyedness in right-handed people and of left-eyedness in left-handed people. He states that he cannot agree with those who would regard the prevailing dominance of one eye as an important factor in producing motor anomalies and visual disturbances.

In the second part of the paper the fusion of similar objects, or stereopsis, is discussed. Dr. Duane stated that in effecting the perception of depth and solidity several factors enter, and the relative importance of these varies greatly according to the circumstances. He divided them into extrinsic, or those dependent on the character of the things seen, and intrinsic, or those dependent on the functioning of the eyes themselves. As thus divided the factors are: extrinsic—distinctness of outline, effects of light and shade, overlapping contours and motion parallax; intrinsic—size of retinal image and accommodative effort; a third group is included wherein binocular factors alone apply—dissimilarity of retinal images, convergence effort and physiologic double images. Each is mentioned in detail. They have already been covered in this review under the mention, in abstract, of LeConte's drawing of projection from the binoculus.

To sum up the entire matter of binocular vision and projection, one obtains thereby a notion of the shape of objects, their relative and, to a certain extent, their absolute, size, and their position with regard to one another either in a transverse or in a fore-and-aft plane. Postural elements give one the notion of the erectness of objects, and tell one whether they are straight ahead, to one side, above or below, and the two elements combined tell one the distance of the external objects viewed.

SPAETH, Philadelphia.

THE EXAMINATION OF PERIPHERAL OCULOMOTOR PARALYSES. JEAN NORDMANN, Rev. d'oto-neuro-opht. **9**:16 (Jan.) 1931.

The physiology of the ocular muscles is discussed and a detailed method of examination for oculomotor paralyses is described. The following points are brought out: The lateral action of the four vertical muscles (superior and inferior recti) is minimal; their vertical action in raising and lowering the eyes varies with the position of the globe; the superior rectus is an elevator and an internal rotator with the globe in adduction, but with the globe in abduction its rotating action is lost; the inferior rectus is a depressor and an external rotator with the globe in adduction, but only a depressor when the globe is in abduction; the superior oblique is a depressor, especially with adduction of the globe, and an internal rotator, especially when the globe is in abduction; the inferior oblique is an elevator with adduction, and an external rotator with abduction of the globe. In other words, a rectus muscle acts in a vertical sense, especially during abduction of the globe, and an oblique muscle has the same function, especially during adduction.

Two laws must be remembered: (*a*) that lowering of the gaze causes convergence and (*b*) that inclination of the head toward a shoulder excites the muscles that turn the superior part of the vertical meridian of the cornea toward the opposite side.

The objective signs of oculomotor paralysis are strabismus, diminution of motility and an inclined position of the head. Fixation with the paralyzed eye always provokes the greatest strabismic angle. A sursumvergent or deorsumvergent paralytic strabismus indicates paralysis of a vertical motor muscle.

In examining the ocular motility it is an error to cause the patient to regard an object brought near to the eyes, owing to the complicating effect of convergence. It is better to turn the head of the patient in different directions while he fixes his gaze on a lamp at a distance of 5 meters. It often happens that in repose there is no deviation of the eyes, and yet there is complaint of diplopia and vertigo. A patient with oculomotor paralysis keeps his head in a position that eliminates the necessity for action of the paralyzed muscle; hence the rule that

the head is turned in the direction of the action of the paralyzed muscle. A better rule is that the patient chooses the position of the head that most easily gives him binocular vision. For example, the superior oblique has been considered to be a depressor and an abductor, and when it is paralyzed the head would be lowered and turned toward the side of the diseased eye. In reality, the head is always turned toward the side of the sound eye, because when this is done the paralyzed eye is placed in abduction. Since in abduction the superior oblique has almost no vertical action, its vertical action is thus eliminated. In some cases the head is inclined toward the shoulder on the side of the sound eye. Complete elimination of the action of the superior oblique is obtained by lowering the head, turning it toward the sound eye and inclining it toward the shoulder on that side. Inclination of the head toward the shoulder on the side of the sound eye is found in paralysis of muscles inserted in the upper part of the globe (superior rectus and superior oblique), and toward the shoulder on the side of the paralyzed eye in paralysis of the inferior muscles — inferior rectus and inferior oblique.

By combining this examination with a study of the strabismic angle and with investigation of the ocular motility, a precise diagnosis may be made.

A subjective examination should be made only after a thorough objective examination. The subjective symptoms are false projection and diplopia. False projection occurs in the direction of the action of the paralyzed muscle. It is revealed by asking the patient to touch an object with the finger while his sound eye is closed. The examination for diplopia should be made only to confirm the results of the objective examination. The method of Landolt (having the patient look at a stable light while his head is put in nine different positions) should be followed. As a source of light the author uses a lamp with a rectangular filament. If paralysis of the four horizontal muscles is suspected, the lamp is so placed that the filament is vertical; if paralysis of the eight vertical muscles is looked for, it is placed in a horizontal position. A deep red glass is always placed before the right eye. The character of the diplopia, that is, whether it is crossed or homonymous will indicate whether an adductor or an abductor muscle is involved; the distance between the two images will increase in proportion to the degree that the gaze is turned in the direction of the paralyzed muscle, thus indicating which eye is affected. Hence, if the distance is increased and there is homonymous diplopia while looking to the left, there is paralysis of the left external rectus; if there is crossed instead of homonymous diplopia, paralysis of the right internal rectus is present.

When paralysis of one of the vertical muscles is suspected it is not necessary to know whether the diplopia is crossed or homonymous. The head of the patient is raised and lowered. If diplopia appears or increases on looking downward, a depressor muscle is paralyzed; if this occurs on looking upward, paralysis of an elevator is present. The image in the affected eye is lower when there is diplopia on looking downward and higher when there is distinct diplopia on looking upward. These two procedures determine whether an elevator or a depressor muscle is paralyzed and which eye is involved. To ascertain which of the two elevators or depressors is at fault, the following technic is employed: Let it be assumed that the result of the examination points to paralysis of a depressor muscle in the right eye. The head of the patient is inclined backward, the gaze is directed downward and the head is turned to the right and to the left, while the gaze is fixed on the light. Attention is directed solely to the vertical distance between the two images. If this distance is increased when the globe is lowered and in adduction, the superior oblique is paralyzed; if the distance increases with abduction, the inferior rectus is incriminated. The same principles apply to investigation of an elevator muscle. The diagnosis may be verified by having the patient observe the degree of inclination of the images, utilizing the fact that there is antagonism between the elevator or depressor action of the vertical motors and their action in rotating the globe around a horizontal axis.

In the majority of cases an unquestionable diagnosis may be arrived at by the foregoing procedures; but where there is contracture of the antagonist, the vertical distance between the images remains the same with both lowering and elevating of the gaze. If it is known which eye is affected, the muscle at fault may be discovered by the fact that the distance varies with adduction or abduction. If the eye that is paralyzed is not known, the diagnosis between paralysis of the superior oblique of one eye and of the superior rectus of the other may be resolved by bending the head to the shoulder and observing the compensatory movements of the eyes. The distance between the images increases: (*a*) by inclination to the right shoulder, when there is paralysis in the right eye of the superior rectus or the superior oblique or in the left eye of the inferior rectus or the inferior oblique; (*b*) by inclination of the head to the left shoulder, when there is paralysis in the right eye of the inferior rectus or the inferior oblique or in the left eye of the superior rectus or the superior oblique.

By this systematic method of examination many atypical cases will be eliminated, and one will be impressed by the frequency of paralysis of the fourth pair of nerves.

DENNIS, Colorado Springs, Colo.

ALCOHOL AND THE CENTRAL NERVOUS SYSTEM. YANNI TSIMINAKIS, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **33**:24 (Feb.) 1931.

After commenting on the relative rarity of reports as to the effects of alcohol on the brain, Tsiminakis describes in detail the pathologic observations in three such cases.

CASE 1.—A man, aged 58, was infected with syphilis at 35; at 45, he was poisoned by carbon monoxide, and thereafter suffered from severe pains (neuritic?). Three years before death he was admitted to the hospital, where he was subjected to malarial therapy. During the last three years of life he showed poor memory, poverty of perception, mental torpidity and a general slowing down of all intellectual faculties. Owing to the negative observations in the cerebrospinal fluid and the history of chronic alcoholism, the case was diagnosed clinically as a "chronic alcoholic Korsakoff syndrome." The absence of objective sensory disturbances of alcoholic neuritis during life, however, and the presence of a progressive rigidity of the lower limbs, which had persisted for years, led the pathologist to question the diagnosis of an "alcoholic Korsakoff syndrome." To add further to the difficulties in diagnosis was the fact that there had also been a history of carbon monoxide poisoning. It was also difficult to determine whether or not the psychic component of the Korsakoff syndrome was an exogenous type of reaction due to carbon monoxide poisoning, to alcohol, or to both. That carbon monoxide poisoning could not be excluded as a pathogenic factor was proved by the definite pathologic changes in the central nervous system indicative of gas poisoning.

CASE 2.—A merchant, aged 39, was admitted to the hospital with a history of chronic alcoholism. On examination, he showed evidences of an acute disease of the spinal cord in the form of a transverse lesion in the midthoracic region, below which there was marked flaccidity of the limbs with the usual reflex and sensory disturbances found accompanying such lesions. In addition, he also presented features of a typical chronic alcoholic Korsakoff psychosis. Death was due apparently to the disease of the spinal cord.

CASE 3.—A patient had been suffering from "alcoholic epilepsy" for years. As he advanced in age the epileptiform seizures ceased, and there began to appear definite evidences of alcoholic polyneuritis with a Korsakoff-like mental symptom complex. A careful study of his mental reactions, however, led Tsiminakis to believe that the mental picture was not that of a true Korsakoff syndrome, but one of simple dementia secondary to epilepsy, although alcohol also played an important pathogenic rôle in the psychosis.

The pathologic changes in the central nervous system in the three cases are summarized as follows:

In case 1, there was diffuse involvement of the entire central nervous system. The process was predominantly degenerative, and involved especially the ganglion cells, regardless of their location. The cells were swollen and showed coagulation of the plasma with subacute fatty degeneration. In case 2, the parenchymatous changes were neither as severe nor as diffuse as in case 1. The degenerative changes in the cells ran parallel with a pathologic process in the blood vessels and glia, which was especially marked around the third and fourth ventricles and less in the periaqueductal region. The process seems also to have extended to the caudal levels of the medulla oblongata, to the substantia reticularis, to the basal portions of the hypothalamus and to some extent to the striopallidal ganglia. Intense as the degenerative process in the cells was, it was not as marked as the changes in the blood vessels and glia. Two types of changes were observed in the blood vessels: (1) excessive dilatation of the larger vessels, especially the arterioles, and also of some of the precapillaries, and above all of the venous branches; (2) a striking increase in the number of capillaries, with proliferation and a certain amount of capillary fibrosis. In addition to these changes, the walls of the blood vessels also showed degenerations in the form of homogenization, destruction of nuclei and proliferation. These changes were especially marked in the walls of the larger blood vessels. No evidences of inflammatory infiltrates were observed. In the areas in which the blood vessels were dilated, more or less extensive hemorrhages were seen, especially around the third ventricle in the region of the nucleus paraventricularis. Another large hemorrhagic area was found in the dorsal angle of the oral third of the fourth ventricle at the point of transition between the medulla oblongata and the cerebellum, i. e., dorsal to the nucleus of Bechterew. Hemorrhages of this type were also observed in the velum medullae and in the nucleus tecti. There was a marked hyperplasia of the neuroglia in the areas in which the blood vessels appeared dilated. The changes in the glia were more diffuse, but no rosets or nodular formations were present, so that the glial hyperplasia could not be regarded as a secondary vascular effect.

The diffuse changes in the ganglion cells in case 3 were not as marked as in case 2, although they were of the same nature and apparently were not due to vascular changes. The changes in the neuroglia and the vascular dilatations were also of the same nature, but the hemorrhages seem to have been less marked toward the fourth ventricle. The difference in the entire pathologic process was therefore a quantitative one, except for an accumulation of a dark brownish granular pigment in many of the ganglion cells. This pigment consisted of cellular impregnations, which were arranged concentrically in the cells around vessels surrounded by hemorrhagic areas, but they bore no relation to any particular vascular supply. In a few areas, these granules were also observed in the walls of blood vessels, while in other areas they were scattered throughout the brain tissue, and in still others they were observed in the glia cells.

From this investigation, Tsiminakis concludes that alcohol, not unlike carbon monoxide, has a certain affinity for various territories of the central nervous system, in which it produces certain typical changes: (1) changes in the vascular apparatus (increase in the capillaries as an expression of a certain productive stimulation of the mesoderm) and (2) hemorrhages of the type usually observed in classic hemorrhagic poliencephalitis. The pathologic picture depends to a great extent on the respective intensity of these two types of lesions in combination. It is obvious, then, that toxic processes may produce similar qualitative and quantitative, though not identical, changes in the central nervous system. On the other hand, neither the character nor the site of the lesion is positive evidence as to its clinical effects, because identical psychic syndromes seem to have at their bases entirely different anatomic substratums, and clinically dissimilar pictures may occur in the presence of identical pathologic processes in the central nervous system.

KESCHNER, New York.

INVESTIGATIONS OF THE ACTION OF BULBOCAPNINE IN MAN. U. DE GIACOMO, Riv. di pat. nerv. **36**:423 (Nov.-Dec.) 1930.

Bulbocapnine is an alkaloid extracted from Corydalis cava. Its chemical formula was established in 1902 by Gadamer. Buscaino believes that this formula enters into the large one of the cyclic ethyl amine of Lowe. Peters, in 1904, and recently Fröhlich and Meyer, 1920, have studied the physiologic action of bulbocapnine, pointing out its cataleptic action. De Jong, 1923, started the first systematic investigation of this alkaloid. Bulbocapnine has been studied in all types of animals, especially by de Jong and Baruk. There is a consensus as to the cataleptic action of the drug in the various types.

The first attempt to study bulbocapnine in man was made in 1924 by de Jong and Schaltenbrand, who injected it into three normal persons, producing only a slight somnolence associated with a sense of fatigue. In 1926, F. H. Loewi injected, hypodermically, 100 mg. of the alkaloid into twenty patients, ten of whom had cases of parkinsonism, and concluded that bulbocapnine has a sedative influence on the tremor, as it produces some kind of an exaggerated muscular rigidity. In the same year, Fleischhäcker was able to confirm the beneficial action of bulbocapnine in postencephalitic tremor. In 1928, Henner studied the action of bulbocapnine by using, among others, two normal subjects, one patient with a cerebellar syndrome of traumatic origin, and two with postencephalitic parkinsonism. In all five subjects, Henner explored the vestibular, cerebellar and extrapyramidal functions. The doses used were from 200 to 500 mg., injected intramuscularly. Henner's conclusion was that bulbocapnine increased the parkinsonian manifestations, especially the muscular plasticity of the cataleptic phenomena. The postural reflex becomes stronger, but the pathologic synergia becomes more marked. In 1929, Hill reported some improvement in cases of disordered behavior in postencephalitic persons. In 1930, Delamas Marsalet studied the postural reflex in persons with parkinsonism following an intramuscular dose of 200 mg. of bulbocapnine. Twenty minutes after the injection, the reflex became much greater, whereas the tremor showed a tendency to diminish.

De Giacomo has investigated the action of bulbocapnine in man through the use of injections of 100 mg. intravenously. His object was to establish whether bulbocapnine produces a clinical picture comparable to a parkinsonian condition or to a catatonic condition. Another aim was to investigate the reaction in patients with dementia praecox with catatonia or catalepsy. He also used feebleminded subjects to study the postural reflexes and variations of pulse rate, blood pressure and various secretions.

Four or five minutes following the intravenous injection, the patient begins to yawn and manifest a certain somnolence. At the same time, absolute immobility develops, with loss or, at least, great diminution of motor initiative. The patients who are talkative become mute, and even the most restless ones fall into a state of complete inertia. There were two exceptions; two patients, after from ten to forty minutes of somnolence, had a manic attack with hallucinations, following which they again became somnolent. Associated with somnolence there is a considerable congestion of the head, with tachycardia and an increased blood pressure. In a sitting position the whole body acquires a flexed position. Ten or twenty minutes after the stage of somnolence, the stage of catalepsy begins, the tachycardia disappears and psychomotor sluggishness develops, with a tendency of the head and trunk to assume attitudes in flexion. Flexibilitas cerea may develop at this stage. The postural reflexes, which appear diminished in the first ten or fifteen minutes, increase during the stage of catalepsy. After from forty-five minutes to two hours the condition of the patient returns to normal.

De Giacomo insists on the variability of the reaction from person to person and from one experiment to another. He also points out that following an injection of bulbocapnine there is diminution of the calcium content of the blood and an increase of the potassium content. From a study of the loss of motor initia-

tive, the catalepsy, negativism, expressions of the face, the tendency toward attitudes of flexion, the local and general postural reflex, chronaxia, electromyographic curves and vestibular stimulation, he believes that the syndrome has close analogies with both the parkinsonian syndrome and the catatonic state. This analogy is not surprising if one recalls the work of Buscaino, Dide, Guiraud, Kleist, Frankel and Sommer, who have established that in catatonia there is disturbance of the tonic innervation of striated muscles owing to involvement of the extrapyramidal centers.

However, the syndrome due to bulbocapnine is more comparable to catatonia because of the psychomotor sluggishness and the loss of mimic expression; a more inconstant manifestation is catalepsy. It differs from catatonia because of the absence of psychic dissociation, negativism, stereotyped movements, mannerisms, echopraxia, echolalia, etc. The syndrome of bulbocapnine differs from the parkinsonian syndrome because of the absence of two fundamental symptoms; real muscular rigidity and loss of normal associated movement. According to de Giacomo's impressions, the bulbocapnine syndrome is therefore closer in its fundamental features to the catatonic syndrome than to the parkinsonian one.

FERRARO, New York.

I. THE REACTION TO POSTERIOR PITUITARY EXTRACT (PITUITRIN) WHEN INTRODUCED INTO THE CEREBRAL VENTRICLES. HARVEY CUSHING, Proc. Nat. Acad. Sc. **17**:163 (April 15) 1931.

Herring (1908) first described hyaline bodies in the neurohypophysis, believing apparently that they were the secretory product of the epithelial portion of the posterior lobe known as the pars intermedia. Globules appeared to go toward the tuber cinereum and in favorable histologic preparations could be seen passing between the bodies of the ependymal cells to enter the infundibular cavity. Cushing and Goetsch (1910) supported the conception (1) by showing that occlusion of the pituitary stalk served to dam back the secretory product in the pars nervosa, and (2) by demonstrating that the active principle of the lobe was detectable in the spinal fluid. Histologic confirmation of Herring's discovery has been made and has shown that the cells in question, under a nervous stimulus, disgorge their ripened cytoplasm into the pars nervosa and that the extruded product undergoes hyalinoid transformation during its migration into the tuber cinereum. Histologic study has also shown that the posterior part of the pituitary body receives a rich nerve supply from the thalamencephalic centers. The extrusion of hyaline globules into the ventricles has also been observed histologically.

Physiologically, it has been shown: (1) that a substance resembling extract of the posterior lobe is often demonstrable in normal ventricular and cisternal, but not in lumbar, fluids; (2) that it may be increased by the administration of certain organic extracts as well as of drugs, particularly those producing diuresis; (3) that it disappears after hypophysectomy or occlusion of the pituitary stalk; (4) that it is increased by emotional stimuli, and (5) that it is augmented by direct stimulation of the hypothalamus or tuber. McLean expressed the belief that this substance is absorbed initially by the vascular route, finding its way to the cerebrospinal fluid through the choroid plexuses. Karplus was of the opinion, however, that the active principle of the posterior lobe is discharged, at least in part, into the ventricular fluid.

Cushing injected solution of pituitary directly into the ventricles in human beings and found that the extract thus injected caused a prompt response characterized by intense flushing from vasodilatation, profuse perspiration, retching and vomiting, salivation, a marked fall in body temperature and a lowering of the basal metabolic rate.

There are two possibilities regarding the action of the extract: (1) resorption into the blood stream, and (2) the direct stimulation of hypothalamic nuclei by diffusion of the substance through the ependymal lining of the third ventricle. Of these, the latter is the more probable.

II. The Similarity in the Response to Posterior Lobe Extract (Pituitrin) and to Pilocarpine When Injected into the Cerebral Ventricles. Harvey Cushing, Proc. Nat. Acad. Sc. **17**:171 (April 15) 1931.

Solution of pituitary, when injected into the ventricles, produces a reaction so similar to that of pilocarpine that Cushing decided to make comparative studies of the two drugs. Both drugs produce flushing, sweating with salivation and lacrimation, retching and vomiting. The chief differences between the two lay: (1) in a more marked vagal effect from pilocarpine, with continued retching and vomiting, as compared with only a brief period of nausea with solution of pituitary, and (2) in a more pronounced fall in body temperature from pituitary. Both of these substances give reactions that suggest a parasympathetic (bulbar) rather than a sympathetic (thoracolumbar) stimulation that is central in origin.

III. The Action of Atropine in Counteracting the Effects of Pituitrin and of Pilocarpine Injected into the Cerebral Ventricles. Harvey Cushing, Proc. Nat. Acad. Sc. **17**:178 (April 15) 1931.

Solution of pituitary and atropine, when injected into the ventricles, produce similar effects. Since atropine is an antidote to pilocarpine it was thought that if the reaction of pilocarpine in the ventricle is checked by atropine a similar reaction might be expected for pituitary if the two substances operate through the same nervous mechanism. It has been observed that, when a patient is rendered unduly uncomfortable from recurrent retching and vomiting after pituitary, an injection of atropine and morphine effectually checks the reaction. Cushing found that atropine whether given subcutaneously or previously introduced into the cerebral ventricles, appears completely to counteract the customary effects of pilocarpine and pituitary when administered by way of the ventricles.

Alpers, Philadelphia.

Investigation on the Changes in the Alkali Reserve of the Blood Plasma, of the Urinary Hydrogen Ion Concentration, and of Frequency of Convulsive Seizures Following Administration of Anticonvulsive Drugs and Calcium Chloride in Epileptic Persons. F. Di Renzo and A. Vitello, Riv. di neurol. **4**:1 (Feb.) 1931.

Following Sabbatani's observations concerning the importance of calcium as a regulator of neuromuscular excitability and the fact that hypocalcemia has been found in various types of tetany and infantile spasmophilia, it has been thought that the crises in these diseases were due to a deficiency of calcium in the plasma of the body tissues. This conception finds support in the facts that: (1) in spasmophilic children, especially during the attacks, there is a deficiency in the calcium of the cerebral cortex and the output of calcium exceeds the intake; (2) with the cessation of the attacks there is an increase of calcemia, not only in spasmophilic subjects but also in epileptic ones; (3) in animals suffering from tetany due to removal of the parathyroids there is a considerable hypocalcemia; (4) with the administration of calcium in such subjects it is possible at times to notice a diminution of the number of attacks and a diminution of neuromuscular excitability.

On the basis of such observations, calcium has been used as a therapeutic measure in epilepsy. The results, however, are not encouraging. The reason for this failure may be that in order to act properly on neuromuscular excitability the calcium must be present dissociated as a free ion. All the calcium in the organism bound to the various tissues is, therefore ineffective. In order to liberate this calcium from the tissue with which it is bound it is essential to modify the electrolytic equilibrium that occurs when the hydrogen ion concentration is modified, that is, when there is a certain acidity of the medium. It was thought that the amount of calcium ion in the plasma is increased by procedures apt to produce acidosis, because studies of epilepsy have revealed in the plasma an alkalosis with a con-

comitant diminution of the calcium ion in the blood plasma preceding the seizure. Following the seizure, the acid-base equilibrium returns to normal, and a normal amount of calcium ion is again found. It follows therefore that therapy based on producing acidosis has the indirect effect of increasing the amount of calcium ion, which would produce a diminution of the neuromuscular excitability.

Such an acidosis has been secured either through the administration of drugs that provoke the liberation of acids in the plasma (calcium chloride and ammonium chloride), by the administration of free acids (hydrochloric acid, lactic acid or phosphoric acid), or by an appropriate diet rich in fat and poor in carbohydrates. It seems that the ketogenic diet in epilepsy in some cases has reduced the number of convulsive seizures.

With these facts in mind the authors have tried to establish whether phenobarbital, a drug often employed in the treatment for epilepsy, has a beneficial effect from a modification of the acid-base equilibrium of the blood plasma, by increasing its acidity. Calcium chloride also was investigated from the same standpoint. The alkali reserve and hydrogen ion concentration were recorded before, during and after administration of the remedies.

The authors conclude that, in epileptic subjects, after treatment with phenobarbital there is a considerable modification of the alkali reserve, which progressively increases in association with a slight increase in the urinary hydrogen ion concentration. The alkalinity increases until a few minutes before the convulsive attack when the alkali reserve decreases abruptly. Whereas, following the use of anticonvulsant drugs there is an alkalosis, following the use of calcium chloride, which does not seem to affect the convulsions and may even, according to some authors, increase them, there are a diminution of the alkali reserve and an increase in the urinary hydrogen ion concentration. These facts are against the hypothesis that alkalosis of the blood determines the explosion of an epileptic seizure because of the diminution of the ion calcium in the blood plasma.

FERRARO, New York.

SYMPTOMATIC PARKINSONISM: PARKINSONISM FOLLOWING CARBON MONOXIDE POISONING. E. BRZEZICKI, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:148 (Oct.) 1930.

This study is based on three personal cases and a review of the literature. The author's conclusions are summarized as follows: 1. A parkinsonian symptom complex may occur in chronic cases of carbon monoxide poisoning. It is not always an irreparable condition which remains stationary or runs a progressive course; it may also be a transitory phenomenon. 2. In a case of parkinsonism following acute carbon monoxide poisoning, the lesions were limited to: (*a*) bilateral symmetrical necrosis of the pallidum; (*b*) moderate destruction of the large ganglion cells of the caudate nucleus; (*c*) cellular changes in the external nucleus of the thalamus; (*d*) changes in the tubera cinerea, and (*e*) minimal changes in the substantia nigra. 3. On the whole, the cerebral cortex was morphologically intact. 4. Changes in the pallidum occurred in: (*a*) the pallidum externum, which, in association with the lesions in the caudate, is the anatomic substratum for disturbances in "movements of expression," and (*b*) the pallidum internum, to which, in view of the slight change in the substantia nigra, the muscular rigidity is attributed. 5. The extensive necrosis in the right pallidum is responsible for the greater severity of symptoms on the left side of the body. 6. The changes in the outer, lower and posterior portions of the external nucleus of the thalamus are regarded as the probable anatomic substratum for negativism and mutism (Kleist). 7. The lesions in the nuclei of the tuber cinereum are the basis of the vegetative phenomena (greasy face, sweating). 8. The necrosis in the oral portion of the pallidum is probably responsible for the rigidity of the upper half of the body, and this may perhaps confirm the theory of somatotopic localization in that nucleus. 9. The large quantities of pseudocalcified deposits found in the pallidum must be regarded as evidences of disturbed tissue metabolism in

this region, and in this sense they are best interpreted as sequelae. 10. The necrosis is due to a confluence of smaller islets of necrosis collaring the veins. As the latter appeared collapsed rather than distended, stasis cannot be considered as a significant factor in the production of the necrosis. 11. The small necroses around the vessels were found at the margins of the pallidum. The veins traversing the internal capsule toward the vena terminalis showed the most marked "collar-like" swellings. 12. As fewer capillaries were supplied to the internal capsule than to the pallidum, and no necrosis was found in the former, it would seem that the theory that only the capillary supply is of great significance in the production of necrosis is not correct. 13. Occasionally, the oral portions of the pallidum are situated in an area supplied only by one large artery (a branch of the anterior cerebral artery). However, the fact that this region also extends to the internal capsule would seem to contradict the theory of special vulnerability of the pallidum. 14. As in the production of the necrosis, the formation of the necrosis cannot be explained satisfactorily on the theory of impairment of the supply of blood, one must assume the existence of some additional, unknown factor, perhaps that of pathoklisis. 15. The possibility must be considered that preexisting syphilis or arteriosclerosis may facilitate the formation of necrosis following carbon monoxide poisoning, especially in view of the fact that most of these cases reported in the literature showed manifestations either of syphilis or of arteriosclerosis. 16. Thus far, it cannot be satisfactorily explained why parkinsonism after carbon monoxide poisoning, as well as after epidemic encephalitis, in most cases requires a latent period for the appearance of the parkinsonian symptoms in spite of the fact that the pathologic changes seem to be irreparable from the very beginning of the disease. 17. The lateral portion of the substantia nigra showed slight disintegration of the ganglion cells. It is also noteworthy that the pallidopeduncular tract was not entirely free from involvement. The author believes that the destruction of the ganglion cells as well as the slight degeneration of the pallidopeduncular tract is secondary to a homolateral destruction of a part of the pallidum.

KESCHNER, New York.

FREUD'S "THE DISCOMFORTS OF CIVILIZATION." A. A. BRILL, J. Nerv. & Ment. Dis. **72**:113 (Aug.) 1930.

This book of 136 pages represents Freud's formulation of the mainsprings of human behavior. Not having felt it himself, Freud seems to have had difficulty in explaining "religiousness." The thing of which we are surest in this world is our ego or self, which is only a surface modification of the id into which it continues. This feeling of separation of the ego from the rest of the world is evolved from childhood. Frequent pains and displeasures help to detach the ego from the outer world. At length the adult ego is only a shrunken remnant of the original all-embracing feeling of identity with the world. This primitive "oceanic" feeling survives in adult life, and according to Freud is a longing for the father. To the average man the precepts and promises of religion give the assurance of protection by a wonderful Father, and being unable to get much satisfaction from art or science, religion becomes a necessity. Mankind also uses powerful distractions, substitutive gratifications and intoxication to alleviate the distress of life. Against the pleasure principle, which activates man, is his whole environment. Pressure of suffering and social inhibition forces men to make moderate demands for happiness and accept the principle of reality. Unrestricted pleasure, voluntary isolation and intoxication are only partially successful in achieving happiness, while sublimation demands special endowments. Even religion cannot keep its promises, and intimidates intelligence. Freud finds three sources of human unhappiness in: (1) the overwhelming forces of nature; (2) bodily frailty, and (3) inadequacy of relationship to fellow beings. It is unlikely that man will be able to alter the first two sources, and what increased power he has acquired over nature has not improved human happiness. The progress of culture, however, has enabled men to live more contentedly together, owing to the fact that the individual has become subordinated to society. Freud sees a similarity between

the cultural progress and the libido development of the individual. The origin of culture Freud finds in the family, which started because genital gratification became a continuous necessity. Living together was determined by the compulsion to work and by the force of love. Like teeth and hair, however, the sex life seems to be in a state of decadence, for culture tends to bind libidinously one individual to the many and inhibits the complete abandonment of two to one another. Culture imposes great sacrifices on man's primitive aggressiveness. Freud further discusses the two prime instincts, ego and sex, and states his belief that besides an instinct to preserve life, there is an instinct to reconduct life to its original organic state of death. Sadism is interpreted as part of this death instinct turned to the outer world. It is the chief obstruction to culture and sex instinct which tend to unite individuals into larger integrations. Hence cultural evolution is a struggle between Eros and death. When the aggressive instinct is turned toward self, the superego or conscience results. The feeling of guilt is due originally to the fear of the loss of the parent's love, the fear of the parent later being transformed to fear of the superego. This problem of guilt, Freud considers the most important in cultural development. Prevention of erotic gratification leads to aggressive inclination toward the persons who disturbed it, and this aggression becoming repressed is transformed into the feeling of guilt. As in the individual, so in the community a superego is developed under the influence of which cultural development takes place. The command to love one's neighbor as oneself is the strongest defense against human aggression, but it is unenforceable and unfruitful. The fateful question for mankind in Freud's opinion is whether cultural development will successfully prevent the predatory and self-annihilating instincts from destroying the most precious possession of the race.

HART, Greenwich, Conn.

THE CALCIUM IN THE BLOOD AND URINE OF PATIENTS WITH DEMENTIA PRAECOX. S. GULLOTTA, Riv. di pat. nerv. **36**:572 (Nov.-Dec.) 1930.

Because of the contrasting reports in the literature as to the amount of calcium in the urine and the blood in cases of dementia praecox, Gullotta has again studied this problem in thirty-two cases and has measured the amount of calcium in the blood serum following the method of Kramer and Tisdall as modified by Clarke and Collip. Considering the normal value as between 10 and 12 mg. per hundred cubic centimeters of blood, Gullotta reports that fifteen of thirty-two cases, 47 per cent, show an increased calcemia. Only in six cases, 18 per cent, is there a diminution of the calcium content. As to the amount of calcium in the urine, taking values between 0.10 and 0.27 Gm. per hundred cubic centimeters as normal, thirteen cases, 40 per cent, show an increase in the elimination of urinary calcium, whereas, in only six cases is there a diminution of this substance.

It seems that there is a parallelism between the amount of calcium in the blood and the amount of calcium eliminated in the urine. In chronic cases, with the exception of four catatonic cases, there was no variation in the values of the calcium in the blood and urine. In initial cases or in cases of relapse there is an increase of calcium in the blood and elimination of the same substance in the urine. A catatonic patient in a condition of rigidity or stupor was the only one who showed a diminution of calcium in the blood, whereas in agitated patients there was always a tendency toward an increase of the figures for calcium.

In order to establish a correlation between the values of the calcium in the blood and the clinical state of catatonia or psychomotor hyperactivity, the author has reinvestigated the amount of calcium after the stage of catatonia or hyperactivity disappeared and concluded that the stage of catatonia and the stage of agitation are accompanied, respectively, by a diminution or an increase in the calcium content of the blood. Gullotta is inclined to believe that the controversy existing in the literature as to the content of calcium in the blood and urine may be due to the fact that the patients have been examined by the various authors under different circumstances, either in a stage of motor inhibition or motor hyper-

activity. He does not believe that the increase in the calcium content of the blood is the result of acidosis.

Because of the fact that in the literature there exist data showing an increase of the calcium content of the blood in the presence of a pathologic change of the liver and because aromatemia and aromaturia are concomitantly present in dementia praecox, which, according to the author, points to an involvement of the liver, Gullotta is inclined to think that the increase in calcium content in the early stages of dementia praecox must be related to an involvement of the liver tissue due to a toxic factor, probably of intestinal origin.

For the decrease in the amount of calcium in the blood of patients in a stage of catatonia, the authors offers another explanation. He refers to some analogies existing between catalepsy and sleep and recalls the observations of Fisher, who believed that during sleep there is a diminution of calcium in the circulating blood because of the collection of the calcium in the diencephalic vegetative centers, and accepts this explanation for the decreased amount of calcium in the blood of catatonic patients. In order to produce an experimental catatonic stage, Gullotta injected bulbocapnine in some patients, with the result that somnolence and catalepsy were experimentally produced. In all cases, Gullotta reported a diminution of the calcium content of the blood accompanied by a concomitant diminution of the potassium content. Under narcosis, produced by a barbital derivative, there is an increase instead of a decrease of the potassium content of the blood.

FERRARO, New York.

A CONTRIBUTION TO THE KNOWLEDGE OF HEMIBALLISMUS. H. UIBERALL and VILMA SAMET-AMBRUS, Ztschr. f. d. ges. Neurol. u. Psychiat. **131**:502, 1931.

Uiberall and Samet-Ambrus reopen the question of hemiballismus on the basis of a case showing this disorder, in which a small hemorrhage was found in the corpus Luysii at necropsy. They enquire whether there is a clinical entity that can be formed from all cases of hemiballismus and whether the corpus Luysii is to be looked on as a vegetative or a motor center.

The patient of Uiberall and Samet-Ambrus was a man, aged 56, who, about twenty-four hours after a light apoplectic attack, developed pronounced involuntary movements of the left extremities. The movements were rhythmic, continuous and sweeping; they involved the entire limb, and consisted of alternate flexion and extension of the limbs in many different directions; it was impossible to influence them psychically, and they persisted during sleep so that morphine was necessary to allow the patient some rest. The movements were so active that the patient developed sores from constant friction against the bed clothes, and died after a week from exhaustion as a result of the hemiballismus. Neurologically, there was some decrease in muscle tonus on the left side and a slight hyperalgesia in the same area. The brain showed a large, old cyst in the cranial portion of the right putamen and pallidum, small areas of disintegration in the striatum and several small foci of softening in the middle third of the putamen. The right corpus luysii was entirely destroyed, except for a small ventromedial portion, by a small fresh hemorrhage. The hemorrhage extended beyond the corpus luysii in several directions. One of the extensions involved the pes pedunculi; another injured the dorsal half of the substantia nigra, and extended into Forel's field H 1.

There has been some question whether hemiballismus is an entity or is a form of hemichorea. Lotmar said that hemiballismus is a hemichorea increased to a hemiballismus. The authors believe that the movements in hemiballismus differ from those of hemichorea, and on the basis of their characteristics believe, with Jakob and Wenderowic, that a diagnosis of a lesion in the corpus luysii is possible. The movements are slower than choreiform movements; they involve the entire extremity and look, therefore, like voluntary movements. Matzdorff identified two components in these movements: turning and waltzing movements of the trunk and extremities, which he looked on as hemiballismus, and chorei-

form movements due to focal lesions elsewhere. The distribution of the movements, their vehemence and their persistence during sleep, occurring as they do in older people, leads quickly to exhaustion and death. Greiff's patient died fifty-six days after the onset of the hemiballismus; Economo's, eight days, and Jakob's, Matzdorff's, and Wenderowic's patients one month after the onset. In the case reported by Uiberall and Samet-Ambrus, death ensued in one week, and in Fischer's case after four days. Schaffer's patient lived two years, and this difference in duration serves as a means of differentiation between an irritative and an outfall phenomenon.

According to Foix and Hillemand, the corpus luysii is supplied by three vessels: the choroid artery, the posterior cerebral and the posterior communicating vessels. This explains the rarity with which the nucleus is involved in softenings. Hemorrhages are also rare, and occur in persons with advanced arteriosclerosis.

The possibility that the movements in question are caused by an injury of the frontopontocerebellar pathway cannot be ruled out by the cases reported.

ALPERS, Philadelphia.

CLAUDE'S INFERIOR SYNDROME OF THE RED NUCLEUS ASSOCIATED WITH PARINAUD'S SYNDROME. H. ROGER and JEAN PIÉRI, Rev. d'oto-neuro-opht. **9**:421 (June) 1931.

Claude's syndrome is characterized by paralysis of the third nerve of one side and a cerebellar semisyndrome of the other side with dysarthria. In the superior syndrome of the red nucleus (Foix), paralysis of the third nerve is lacking. Benedikt's syndrome is also due to a lesion of the lower part of the red nucleus, but it is characterized by an alternating syndrome of paralysis of the third nerve and motor disorders of the opposite side.

A man, aged 41, without significant family or previous history, experienced suddenly an intense vertigo, followed by loss of consciousness for eight hours. This was followed by ptosis in the left eye, paresis of the right leg and dysarthria. A few days later, paresis of the right arm appeared. Examinations of the urine, the blood and the spinal fluid gave negative results. A neurologic examination revealed complete paralysis of the left oculomotor nerve, paresis of upward movement of the right globe, a right cerebellolabyrinthine syndrome, which was more marked in the legs, and a slight pyramidal excitation, characterized by discrete exaggeration of the reflexes of the right limbs, without clonus or Babinski's sign. Walking was difficult on account of a right lateropulsion, and there was pastpointing to the right. In spite of the negative history and Wassermann reaction, antisyphilitic treatment with arsenic was given and was followed by definite improvement.

The cerebellar hemisyndrome is especially characterized by hemiasynergia. There are added, however, disturbances of the André-Thomas series, bearing on tonus and passivity. Giacomo thought that the red nucleus was a center for the transmission and selection of cerebellar impulses, regulated by impulses from the cortex, pallida and thalamus, and Rademaker showed experimentally its influence on muscular tonus, the position of the body and the labyrinthine reflexes. Souques, Crouzon and Bertrand did not believe that a lesion of the red nucleus would account for the pyramidal syndrome, but it is present in the present case.

The coexistence of Parinaud's syndrome is not easy to explain, although it has been noted by others in cases of a unilateral peduncular syndrome and the syndromes of Weber and Benedikt. In van Bogaert's case of the inferior syndrome of the red nucleus, it was present as a ptosis that lasted only a few days. In their case, the authors favor the hypothesis of Parinaud's syndrome because of its persistence. Clovis Vincent reported a typical case of Weber's syndrome with an associated Parinaud's syndrome. He located the lesion a little above the third nucleus at the edge of the mesencephalon and the suboptic region, where the

sylvian aqueduct opens. It was unilateral and did not involve the quadrigeminate bodies. The association of the two syndromes is explained by an extended obliteration of the median peduncular arteries, paralysis of elevation being due to closure of the superior artery, and motoroculi paralysis to obliteration of the median and inferior arteries.

The inferior syndrome of the red nucleus is usually due to a vascular lesion, although cases due to tumor and tubercle have been recorded. The abrupt onset in the present case points to a vascular syndrome—a necrobiotic focus in the territory of the peduncular artery, probably syphilitic. A case due to hemorrhage was published by Alajouanine in *Revue de neurologie* (**1**:125 [Feb.] 1931).

DENNIS, Colorado Springs, Colo.

THE THREATENING MANIFESTATIONS OF PERNICIOUS ANEMIA. Editorial, J. A. M. A. **97**:543 (Aug. 22) 1931.

The contribution represented by the brilliant discovery of the effect of liver therapy on the management of pernicious anemia should not be allowed to obscure some of the unsolved mysteries of the disease. It is, of course, extremely gratifying to know that before the advent of the liver dietary the outlook in pernicious anemia was grave and recovery was rare, whereas today the prognosis is much better. Liver and its extracts have been used for only a few years. It becomes imperative, therefore, not to allow the early enthusiasm to awaken unwarranted hopes in every instance, and particularly desirable to continue intensive studies on the problems of the disorder. Pernicious anemia has been defined (McCann, W. S., and Maitland-Jones, A. G., in Cecil: Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1930) as a grave progressive disease interrupted by remissions "occurring without any discoverable cause whatever." It is characterized by certain changes in the blood and blood-forming organs, the central nervous system and the gastro-intestinal tract.

Liver therapy has been concerned primarily with hematologic features. The familiar achlorhydria is apparently not altered thereby; and of late the ever-threatening menace of the sclerosis in the posterior and lateral columns of the spinal cord and the neurologic symptoms has loomed up larger. Carey (Carey, J. B.: Pernicious Anemia with Fatal Termination During a Liver Diet, *Arch. Int. Med.* **47**:893 [June] 1931) has stated that, before the advent of liver in the treatment for pernicious anemia, patients died in any of several ways. They became the victims of some intercurrent infectious accident, just as any patient might. They died slowly or rapidly of a progressive anemia which none of the then known therapeutic procedures could check. They died as the result of the progress of the lesions of the cord to the condition which can be classed as "tabetic"; i. e., with paralysis of the extremities, rectum and bladder and with trophic disturbances. Carey utters the warning that liver therapy apparently has no effect on the ultimate outcome in every case of pernicious anemia.

It is too soon to begin to be hopeful that liver substances can indefinitely check the progress of the disease. In considering the result of liver therapy with the idea of deducing an etiologic hypothesis, it must not be forgotten that achylia and sclerosis of the spinal cord are integral parts of the syndrome and that these changes are apparently unaffected by liver. In certain cases, Carey continues, it is evident that one must expect death as the result of the progression of disease of the spinal cord, in spite of a relatively good condition of the blood. In other cases, the blood-forming organs become incapable of further regenerative effort, perhaps as a result of the age of the patient, or even conceivably in younger patients because of exhaustive overstimulation. Finally, there are patients with an aplastic marrow who cannot become stimulated initially. As Carey says, in order to deduce from any method of therapy an etiologic hypothesis, one should not be too dogmatic until some effect is demonstrated on the whole clinical picture rather than on a single phase of the condition.

THE CENTERS OF THE HYPOPHYSIS CEREBRI. R. M. MAIMAN, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:666, 1930.

There is great interest in the question of the connections of the diencephalon and hypophysis, especially since it has been shown that diseases of the hypothalamus may produce the same picture as hypophyseal diseases. Aschner's investigations on glycosuria, those of Krehl and Isenschmied on temperature regulation, those of Leschke and Schmeider, and of von Grafe on water metabolism and those of Camus and Roussy on polyuria demonstrate the existence of vegetative centers in the hypothalamus, injury of which causes "hypophyseal" symptoms.

Clinical and experimental data lead one to believe that the hypophysis and the base of the diencephalon form a unitary system. Kary (1924) destroyed the hypophysis and found degeneration (1) in the gray substance of the tuber cinereum and (2) in the ganglion supra-opticum. Pines (1925) asserted on the basis of studies by Cajal's silver methods that the anterior part of the hypophysis contains sympathetic fibers coming from the carotid plexus, and that the posterior half contains fibers coming from a nucleus in the lateral part of the base of the diencephalon; an unmyelinated bundle of fibers which descends through the infundibulum, goes to the posterior lobe of the hypophysis, forms a dense bundle there and penetrates also into the middle lobe. He called this tract the tractus hypophyseus and the nucleus of origin the nucleus hypophyseus. The latter corresponded to the nucleus paropticus, supra-opticus and ganglion opticum basale meynerti. Greving (1926) reported that the posterior lobe of the pituitary is in connection with the nucleus supra-opticus by means of the tractus supra-opticus hypophyseus. He could find no fibers of this tract in the anterior or middle lobes. Stengel decided that a large part of the fibers in the neurohypophysis comes from the nucleus supra-opticus, but that a part of the fibers of the posterior lobe has origin in the mesial group of spindle-shaped cells in the floor of the third ventricle.

Maiman destroyed the anterior lobe of the hypophysis in three dogs, the posterior and middle lobes in three dogs and both anterior and posterior lobes in four dogs. Injury to the anterior lobe resulted in no changes in the hypothalamus. The changes in this region followed injury to the middle and posterior lobes only. The nucleus showing degeneration was the nucleus supra-opticus, and this nucleus alone. The nucleus tuberi, nucleus paraventricularis and periventricularis, nucleus mamillo-infundibularis and nucleus perichiasmaticus were all untouched after injury of the posterior lobe of the hypophysis. The nerve cell changes in the nucleus supra-opticus were characterized by a chromatolysis. In cases in which the anterior lobe of the hypophysis was removed, chromatolysis was observed in the cells of the superior cervical ganglion; whether this was present after injury to the posterior lobe was not observed.

The middle and posterior lobes of the hypophysis are therefore innervated by the nucleus supra-opticus, while the anterior lobe receives its nerve supply from the carotid plexus.

ALPERS, Philadelphia.

PATHOLOGY OF MULTIPLE SCLEROSIS. MASAMICHI TOYAMA, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **33**:74 (Feb.) 1931.

Twelve cases of multiple sclerosis were examined histopathologically. Acute lesions were found in every case, regardless of the duration of the disease, which varied from six months to eighteen years. Three forms of acute lesions could be distinguished: 1. In Marchi preparations the sections showed tissue completely filled with fatty granular cells which stained black with osmium. 2. Similar cells, seen only at the margin of the lesions, mostly on one side of the lesions. 3. No such foci of osmium-stained granules were observed in the sclerotic patches themselves, although they were present in the sheaths of the blood vessels within as well as without the patches. In addition to these granular cells stained black with osmium, there were seen in some cases granular cells near the center of the sclerotic patches; these cells appeared pale and did not take the osmium stain.

When these sections were stained with scarlet red, many more granular cells were found than appeared to be present with the osmium stain. The three types of lesions described could also be distinguished when the sections were stained with scarlet red. Finally, there were some cases in which the patches showed only sclerosis, but no trace of a granular cell.

The patches in the spinal cord appeared more sclerosed than those in the brain. The former only occasionally showed accumulations of granular cells. In the cases of longer duration the sclerosis was more complete in the cord than in the brain. When acute lesions were found in the brain, they were usually most marked near the ventricles. It must, however, be emphasized that in very old cases a recent lesion could be found here and there in the cord. In this connection the author points out the great difficulty that one may encounter in attempting to determine the "age" of a lesion. As a rule, the presence on the blood vessels of granular cells that take only the scarlet red stain may be regarded as evidence that the process is a chronic one. When, however, a lesion presents evidences that acute destruction of tissue is still going on, and that there has been no attempt to carry off the products of tissue disintegration, it may be assumed that the process is a more recent one.

The determination as to whether the clinical manifestations run parallel with the progression of the pathologic process offers almost insurmountable difficulties. In most cases the clinical picture can be well correlated with the severity and long duration of the lesions found in the cord. As a matter of fact, in a few cases with signs and symptoms of terminal progression recent lesions were found in the brain. Positive evidence, however, of the coincidence of clinical progression with the appearance of recent lesions is not always available. But this is not surprising if one takes into consideration the nature of the disease. It is noteworthy that in two cases with no clinical evidences of progression no acute lesions were found, and in two cases of long duration with definite signs of clinical progression very acute lesions were found.

KESCHNER, New York.

ADEQUATE ELECTRICAL STIMULI FOR POSTURE AND MOVEMENT. GRACE BRISCOE, J. Physiol. **71**:292 (March) 1931.

Muscle has two main functional activities, the holding of posture and the carrying out of movements. In the investigation reported an attempt has been made to reproduce these differing forms of activity by supplying the peripheral motor nerves with suitable electrical stimuli. The muscle chiefly used was the quadriceps of the cat. The neon lamp flashing circuit was used to supply the iterative stimuli. The blood supply of the muscle was interfered with as little as possible. Dial-Ciba and ether, either alone or combined, were the anesthetics used.

The results of these experiments show that in order to obtain satisfactory postural contractions prolonged for periods running into hours the following experimental conditions are necessary: (*a*) a low rate of stimulation; (*b*) a depth of anesthesia in which the corneal reflex is still present; (*c*) an adequate blood supply to the muscle. When conditions (*b*) and (*c*) have been provided, the deciding factor is the rate of stimulation. Low rates of stimulation (for example from 20 to 25 a second) will maintain posture for hours; higher rates are suitable for rhythmic phasic contractions. Although the actual rates, the range of rates and the speed of giving way in the postures may all vary with different experimental conditions, the broad principle of the reaction remains the same, namely, that there is a limited range of rates within which full steady posture can be held without sign of fatigue, and that rates below or above this range lead either to tremulous action or to decline of posture. There is no hard and fast line between the stimuli capable of exciting tonic or phasic activities in the muscle. Prolonged postures were obtained under ether anesthesia alone, and dial-Ciba alone, and under a combination of these two drugs.

The artificial postural contractions described in this paper are compared with the reflex postural contractions in decerebrate rigidity and are found to bear a close resemblance to them. The most important similarity is the relative non-fatigability of the two preparations. The action currents detected in postural reflexes and those in decerebrate rigidity occur at a low rate (from 5 to 25). In the peripheral preparations here described, rates of 20 a second were commonly used for posture, and after the posture had been held for a period the rate could be reduced to as low as 14 a second. In both reflex and peripheral preparations the postural contraction is abolished by deep ether anesthesia. Prolonged contraction in both preparations is conditioned by an active circulation. In the peripheral preparation, as in the reflex preparation, it can be shown that the maximal tension of the posturally acting muscle is less than when it is acting physically.

ALPERS, Philadelphia.

THE HEMATO-ENCEPHALIC BARRIER IN ALCOHOLIC INTOXICATION. E. S. LOKSHINA, Medicobiological J. (Russian) **5**:126, 1929.

The permeability of the hemato-encephalic barrier is influenced by various toxic substances, such as the toxins of diphtheria and tetanus. Walter noticed also that there is an increased permeability in certain mental diseases. Changes in permeability were observed by Stern and Baatard in cases of alcoholic intoxication. However, the results obtained by various investigators have been variable.

In the experiments cited by the authors the subjects were rabbits and guinea-pigs. They were subjected to acute and chronic alcoholic intoxication. The permeability was studied by means of colloids such as congo red and trypan blue, and crystalloids such as sodium iodide, bismuth subnitrate, sodium bromide and others. Bismuth was introduced intraperitoneally; the other salts were injected into the vein of the ear in rabbits, and into the carotid vein in guinea-pigs.

The animals were killed from five to ten minutes after the injection of congo red, iodides, picric acid and potassium ferrocyanide. After injections of trypan blue and sodium bromide the animals were killed by bleeding. After injections of bismuth they were killed in sixty minutes. The substances were estimated in the blood and cerebrospinal fluid. The spinal fluid was examined only when it was free from red cells. The brain was carefully washed with solution of sodium chloride. The methods of determination were those of L. Stern.

The results were: (1) Acute intoxications lasting for two or three weeks, lead to a lowering of the barrier with bromide. (2) In chronic intoxication the modification of the barrier depends on the length of the period of intoxication. (3) Intoxications lasting for from one to three and one-half months lead to decreased permeability for bromides; the same holds true of salicylates and cyandies. There is an increased permeability, however, to bismuth. (4) With longer periods of intoxication the permeability to bromides is even more decreased. (5) Intoxication with alcohol for more than six months leads to a complete occlusion of the barrier to sodium cyanide, sodium bromide and sodium salicylate, a decreased permeability to picric and an increased permeability to bismuth and congo red; sodium iodide and sodium ferrocyanide remain without change.

KASANIN, Boston.

THE "PERMEABILITY QUOTIENTS" OF CALCIUM, CHLORIDE (TOTAL HALOGENS) AND BROMIDE AND THEIR MUTUAL RELATIONS IN ENDOGENOUS MENTAL DISEASES. H. FLEISCHHACKER and G. SCHEIDERER, Monatschr. f. Psychiat. u. Neurol. **75**:346 (May) 1930.

Parallel determinations of the calcium, chloride and bromide ratios of distribution between the blood and cerebrospinal fluid were made on patients suffering from the common types of mental disorder. The distribution ratio or so-called

permeability quotient of calcium was investigated in seventy-five cases. Most of the determinations were within normal limits, although there was a tendency for the schizophrenic group to show a slight lowering of the calcium level, particularly in the spinal fluid. Most of the chloride ratios were normal. The halogen content of the spinal fluid was more constant than that of the blood. The permeability quotient of bromide was generally somewhat higher in children than in adults, and was apparently independent of the absolute amount of bromide administered. The authors point out that the total halogen content of the spinal fluid does not vary at different levels of the spinal cord, whereas the bromide content is usually greater in the lumbar region than elsewhere. They are unable to explain this phenomenon, but regard it as a warning to proceed cautiously in interpreting the results obtained with Walter's method. In a group of thirty-one patients with schizophrenia, six showed bromide ratios above 3.3. Low bromide quotients were found in a considerable number of patients with dementia paralytica, but the endogenous psychoses did not exhibit characteristic values. There was apparently no relation between the distribution ratios of bromide, chlorides and calcium. The authors come to the conclusion that such electrolytes as calcium and chlorides are unsuitable for the determination of finer variations in the "permeability" of the blood-cerebrospinal fluid barrier.

ROTHSCHILD, Foxborough, Mass.

APPROACH TO STUDY OF HYSTERIA. S. A. KINNIER WILSON, Proc. Roy. Soc. Med. **24**:173 (Dec.) 1930.

Hysteria has undergone various metamorphoses in the course of time. One no longer sees the ecstasies of the Middle Ages nor the "circus horse" of the Salpêtrière. The observation of Morestin that hysterics keep up with the progress of medicine is very apt. The elaborate somatic manifestations of the past are now rare. The former emotional extravagances are contrasted now with a cold, scientific demeanor, while the practical but not less egocentric defensive hysteria is "de rigueur." The instinctive, impulsive reactions have not altered. One can see cortical, infracortical, bulbar and neurosympathetic mechanisms markedly disturbed by hysteria. These former specific criteria of distinction between the organic and the hysteric have lost their specificity because one thinks now in terms of physiologic pictures. It would be clearer if instead of organic and functional one substituted the terms static and dynamic. In the case of epileptic attacks one finds no alterations of the nervous system, but instead can speak in terms of a dynamic stimulus which, at first limited, later draws into activity a wide area of the nervous system. In hysteria also the dynamic elements predominate, while the static elements slip into the background. One sees common physiologic processes in the symptomatic confusion of hysteria just as they lie at the basis of other clearly recognizable diseases; but when one seeks for the pathogenesis, difficulties begin. If one advocates the idiogenic theory of the origin of the symptoms, the sexual origin is ignored. An important rôle is certainly played by the emotional life, but this is not enough. Hysterics are born and not made. Fundamentally, temperament rests on a physiologic and not on a psychologic foundation. Hence the labile reactions and the lack of neuronic cohesion.

HART, Greenwich, Conn.

THE ACTIVATING INFLUENCE OF LIGHT UPON CERTAIN AQUATIC ARTHROPODS. WILLIAM C. STEHR, J. Exper. Zool. **59**:297 (April 5) 1931.

The aquatic arthropods, Asellus communis Say, Cambarus sp., Hyalella knickerbockeri (Bate) (three Crustacea), Ranatra americana Montandon, Belastoma flumineum Say and Lethocerus americanus (Leidy) (three Hemiptera), are quiescent in the dark. They generally respond to sudden illumination by a definite reflex action, usually a swimming movement. After a response to light, a period of recovery in the dark is necessary to obtain a second response in the same time. A ten minute recovery period is sufficient. Temperature and metabolism influence

responses to light. Photoreception, in the adult Hemiptera tested, is through the eye. Blackening one eye of Belastoma has practically no effect on its photic responses. The means, standard deviations and coefficients of variation of the different species show wide variability, due in part to differences between individuals and in part to undetermined influences on the physiologic state of the individuals. There is an inverse relationship between intensity and reaction time in the species studied, which is similar in all. There is a latent period of about 0.6 ± 0.2 second in the reaction time of Lethocerus. The maximum stimulating efficiency of light appears to be much lower for Lethocerus than for the other species. Dark adaptation follows a regular course in Lethocerus, and is complete in about fifty minutes. The results of the experiments are consistent with Hecht's hypothesis of photoreception, but further problems must be solved before making a complete analysis in terms of this hypothesis.

WYMAN, Boston.

ANISOCORIA IN BITEMPORAL HEMIANOPIA EVOLVED FROM ONE EYE. JEAN NORDMANN, Rev. d'oto-neuro-opht. **9**:175 (March) 1931.

It is generally agreed that the pupillary fibers partially decussate in the chiasm. Behr thought that they cross again in the superior part of the optic tract. The fibers found in the left optic tract (from the temporal half of the left retina and the nasal half of the right retina) go to the right pupillomotor nucleus; those in the right optic tract end in the left nucleus, and only the macular fibers are in connection with both nuclei. Thus the fibers from the nasal part of the retina go to the homolateral center, while those from the temporal half cross the median line only once and end in the opposite nucleus. Since each nucleus presides over the pupillary reflex of its own side, it may be assumed that illumination of the temporal half of the retina provokes a consensual reflex and illumination of the nasal half causes a direct reflex. In order to verify this assertion, the author studied five patients with signs of tumor of the hypophyseal region. All were blind in one eye and the other eye showed a temporal hemianopia. Thus, only one temporal hemiretina functioned. In three cases, with feeble illumination the pupil of the blind eye was three times smaller than the other one. One patient was unconscious when examined but the blind eye was correctly indicated by its smaller pupil. In another analogous case, the pupils were equal and anisocoria in favor of the blind eye was present only momentarily. In the fifth case the pupil of the blind eye was larger in spite of many examinations in different positions and with varying intensities of illumination.

DENNIS, Colorado Springs, Colo.

AN UNCOMMON CASE OF CEREBRAL SYPHILIS. E. DE ANGELIS, Arch. gen. di neurol. e psichiat. **11**:359, 1930.

The author reports a case of cerebral syphilis with autopsy and histologic study of the central nervous system. The condition developed in a man, aged 30, with headache and dizziness as the first symptoms; then followed gradual paralysis of all the cranial nerves, which was more severe on the right side (hyposmia, amaurosis, internal and external ophthalmoplegia, paralysis of mastication, hypoacusis, dysphagia, anarthria and atrophy of the tongue); eventually, meningeal symptoms set in, with rigidity of the neck, Kernig's sign, a clasp-knife attitude of the body and general deterioration. The spinal fluid pressure measured 30 (Claude's manometer); the fluid showed: protein, 1.5 Gm. per liter; 50 cells per cubic millimeter, and a slightly positive mastic curve in the syphilitic zone; the Wassermann reaction of the spinal fluid was negative, that of the blood was positive. The patient died in profound cachexia three months after the onset of the first symptoms. Autopsy revealed: a basilar meningitis involving all the cranial nerves; multiple cysts of softening in the right hemisphere; arteritis of the sylvian arteries, especially on the right side; pleural adhesions on the left; terminal

bronchitis. Histopathologic study showed syphilitic arteritis, especially of the right sylvian artery, chronic leptomeningitis of the base, encephalitis of the ventral convolutions of the brain, and neuritis of the cranial nerves. The involvement of all the cranial nerves and the rapid clinical evolution constituted a rare type of cerebral syphilis.

YAKOVLEV, Palmer, Mass.

A CONTRIBUTION TO THE KNOWLEDGE OF THE HISTOPATHOLOGY OF THE SUBSTANTIA NIGRA. M. EMMA, Riv. di pat. nerv. **36**:483 (Nov.-Dec.) 1930.

In order to establish whether lesions in the substantia nigra are specific for certain diseases, Emma has investigated this region in various pathologic conditions, studying particularly the nerve cells and their inclusions, the neurofibrillar reticulum, the pigment, the fats, the iron, the blood vessels and the neuroglia. The conclusions are: 1. In 21 of 65 cases, although clinically there were no signs referable to so-called extrapyramidal disease, the nerve cells, glia cells, connective tissue and blood vessels of the substantia nigra were in a pathologic condition. 2. The lesions mentioned, especially those referable to the nerve cells, recall the lesions described in the substantia nigra in cases of epidemic encephalitis and Parkinson's disease. 3. It follows from the foregoing conclusions that one must be careful in establishing a correlation between the clinical symptoms referable to the extrapyramidal system with lesions located in the substantia nigra. 4. It seems that the substantia nigra reacts in a uniform way to the most varied pathologic stimuli.

The conclusions seem to corroborate the skepticism that was expressed by Rademaker in connection with studies on muscular tonus. Rademaker reported that destruction of the substantia nigra was compatible with an absence of disturbance in tonicity, a fact which the abstractor has reported experimentally in cats and rabbits in which no appreciable disturbance of muscular tonus was detectable though the substantia nigra was entirely destroyed on one side.

FERRARO, New York.

THE HUMORAL EFFECT OF STIMULATION OF THE OCULOMOTOR NERVE. E. ENGELHART, Arch. f. d. ges. Physiol. **227**:220, 1931.

Since Loewi's discovery that the vagus acts on the heart by producing in the periphery a specific chemical substance, it has been shown that the effect of stimulation of the nerves on the peripheral organs is also due to a humoral mechanism (for instance the vasodilator effect of the stimulation of the posterior roots). To confirm Loewi's theory about the internal muscles of the eye, Engvelhart studied the aqueous humor of the eye in cats and rabbits. Under normal conditions, he was not able to find in this humor a substance similar to that produced by stimulation of the vagus ("vagus substance"). After stimulation by physostigmine and light, he found such a substance in the eyes of rabbits, but not in the eyes of cats. Following the injection of physostigmine without stimulating the eye with light, the substance could not be found, or could be found only in very small quantities in the corpus ciliare and in the iris in rabbits and cats. The amount of the substance is considerable, and it is increased after electric stimulation of the oculomotor nerve. It disappears after degeneration of this nerve.

SPIEGEL, Philadelphia.

THE MENTAL CAUSES OF CHILD ACCIDENTS. HERBERT J. STACK, Ment. Hyg. **15**: 283 (April) 1931.

The most important approach to the problem of preventing accidents among children is that of mental hygiene. The mental factors that may represent the underlying causes of accidents include worry, fear, rebelliousness, adventurousness, stupidity and fatigue. Worried children are often anxiously hurrying to get somewhere; they are apt to be less alert. Rebellious children resent safety instruc-

tion and are apt to court danger as a gesture of defiance; adventuresome boys may seek the thrill of jeopardizing their limbs in street traffic. Fatigue commonly underlies accidents, and it is a fact that most accidents to children in the streets occur in the late afternoon. Stupidity bears an uncertain relationship to the danger of suffering an injury; certainly the feebleminded child is more apt to get into trouble than the normal one, but within the limits of normal intelligence it has never been demonstrated that caution and mentality are proportional. The school, the home and the community in general must provide oportunities for real but relatively safe adventure for children and must cultivate in its future citizens a healthy and intelligent respect for danger.

DAVIDSON, Newark, N. J.

IODIN IN EXOPHTHALMIC GOITER. A COMPARISON OF THE EFFECT OF ETHYL IODID AND POTASSIUM IODID WITH THAT OF LUGOL'S SOLUTION. JACOB LERMAN and JAMES H. MEANS, Am. J. M. Sc. **181**:745 (June) 1931.

This work attempts to determine whether the type of iodine compound or the route of entry into the body are factors in the iodine response. In twenty-three patients who were treated with ethyl iodide by inhalation, there was a reduction of more than 10 points in the level of metabolism, the drop varying from 12 to 55 points. In eighteen patients treated with saturated solution of potassium iodide, there was a fall in basal metabolic rate, varying from 16 to 47 points. The response of exophthalmic goiter to ethyl iodide and to potassium iodide is essentially similar to the response to compound solution of iodine. During the period of ethyl iodide or potassium iodide administration, the other symptoms and signs of the thyrotoxic state showed changes as well as the metabolism. It is concluded that iodine produces its characteristic changes in exophthalmic goiter independently of the type of iodine compound or the route by which it gets into the body.

THE EFFECT OF CAFFEINE ON THE CEREBROSPINAL FLUID PRESSURE. PETER G. DENKER, Am. J. M. Sc. **181**:675 (May) 1931.

In a series of fifty cases, mostly neurologic disorders, 5 grains (0.324 Gm.) of caffeine sodium benzoate in a sterile solution in 20 minims (1.23 cc.) of water was injected intravenously, and the manometric pressure of the cerebrospinal fluid was noted every minute. The average fall in pressure for all the fifty cases was 36 per cent, the minimum 8 per cent. In ten control cases, in which a sterile solution of 20 minims of water was injected, no fall in pressure occurred. The mechanism of this reduction by caffeine is discussed according to: (1) its effect on the circulation, (2) the diuretic action of caffeine and (3) the respiratory action of caffeine. It is concluded that caffeine lowers cerebrospinal fluid pressure by its combined pharmacologic actions, rather than by any specific effect on intracranial pressure. The foregoing gives a more scientific rationale for the further therapeutic use of caffeine in conditions of increased intracranial pressure.

HEAD MURMURS. LOUIS P. HAMBURGER, Am. J. M. Sc. **181**:756 (June) 1931.

The necessity of cephalic auscultation is pointed out, and various conditions are discussed. Systolic cephalic murmurs of childhood are probably without pathologic significance. In the acquired intracranial type of arteriovenous aneurysm, a case of a communication between the right internal carotid and cavernous sinus with a head murmur, without the development of pulsating exophthalmos, is unusual. Other varieties of head murmurs of intracranial vascular origin are cerebral aneurysmal angiomas and certain tumors—meningiomas and gliomas. In the extracranial group of head murmurs belong those of the diploe. Another source is that from atheromatous and possibly dilated carotid arteries in which the sounds are transmitted cephalad in the direction of the blood current. Two examples of head murmurs arising in presumably healthy persons without apparently adequate causes are described.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Secretary*

Regular Meeting, April 16, 1931

A. MYERSON, M.D., *in the Chair*

PSYCHIATRIC ASPECTS OF CRIME. DR. WINFRED OVERHOLSER, by invitation.

The legal profession is coming to realize that the old method of mass treatment and the old penal philosophy are not sufficient, and that they are not protecting society to the extent to which they should. One sees the development of individualizing methods, of special institutions, such as those that have been established in Massachusetts and in New York for the treatment of defective delinquents, of reformatories, parole, the indeterminate sentence, etc. The course dealing with the criminal have always been interested, at least in theory, in the mental state of the defendant, but the generally prevalent method of presenting expert testimony has not proved satisfactory.

The great disadvantages of the prevailing system are: 1. Lay initiation of the plea for "recognition" of the case must start with a layman, the lawyer, a court officer, a jailer or a judge — this applies to all states except Massachusetts. 2. The people who testify before the court are partisans — and this applies to most states.

This situation existed in Massachusetts and caused considerable perturbation among the medical profession. It was not until 1921, however, that Dr. L. Vernon Briggs of Boston secured the passage of a law that obviated at a stroke most of the disadvantages. This law provides that in any case in which a person is indicted for murder in the first degree and in any case in which a person is bound over for a felony who has previously been convicted of a felony, the defendant shall be examined before trial by two psychiatrists appointed by the State Department of Mental Diseases. This eliminates partisanship. The examiners are appointed by the state and not by the judges, who may know nothing about qualifications. Again, the procedure is routine, and it is routine in cases in which the issue most often comes up; namely, those cases in which the offense is punishable by death.

In other states, certain courts have established clinics of their own, thus having their own organization; in many instances, courts have clinics at hand on which they may call, these clinics being operated by the state or by some university or organization. In a recent survey, the National Crime Commission found that 9.5 per cent of the courts had some regular psychiatric service.

It is important that the courts should know something of the individual defendant's mental make-up in order that they may properly dispose of the case by fine, probation or commitment to the proper institution. It is absurd for any person to assume that he can set up in advance the period in which reformation or cure will take place. The fallacy of predetermined fixed sentences is fairly well recognized, though not always by legislatures.

It is desirable as well to have psychiatric services available in penal correctional institutions. This fact was recognized before the establishment of clinics, largely due to Dr. A. Warren Stearns, who started this work in Massachusetts in 1914. The value of knowing the prisoner's make-up, the proper industry to

which to assign him and the proper discipline to mete out to him and the value of this information to parole boards are now being recognized.

More recently, Massachusetts has undertaken the examination of convicted persons in the county jails. These may seem to be trivial institutions, but for the United States as a whole, they receive 90 per cent of committed persons, and the prisoners in county jails are notorious repeaters. Then, too, it is important to know what sort of a person is found in such jails and whether his offense, repeated or not, is due to a fault in his own make-up or to a fault of the system.

The proposal of ex-Governor Smith of New York, that the matter of sentences be taken out of the courts and lodged with a special board of sociologic and psychiatric experts, attracted a great deal of attention. Such a proposal is far from realization, but it seems logical in many ways; it would not be at all strange to see such a development in the course of twenty-five years.

It is obviously desirable to fit the treatment to the offender, to make the penal treatment fit the criminal, and this is necessary both in justice to the individual offender and to society. Many persons are being released altogether too soon, whereas others are kept longer than is necessary, because their sentences, prescribed long in advance, require it.

PSYCHIATRIC ASPECTS OF CRIME. DR. EARL K. HOLT, by invitation.

Psychiatric examination and treatment form a part of the regular machinery of juvenile courts, which have been provided in many cities but in few rural communities. Their methods are personal and informal. An attempt is made to treat the individual delinquent's special problems. It would be extremely desirable to have all criminal courts adopt something of the procedure of juvenile courts. The idea of correction and rehabilitation of criminals is new in the history of criminology. There are still many who demand punishment for individual wrongdoing and for the deterrence of criminal behavior, but impartial investigations have shed increasing doubt on the validity of these traditional notions. The deterrent effects of punishment so far as they exist at all are, I believe, general and not specific. Occasionally, a criminal will admit that he avoids a district where prosecution is prompt and vigorous. On the other hand, arbitrary cruelty in the courts, with long, stiff sentences for the unsuccessful criminal who is caught will serve to create hatred against authority, but will neither foster real criminal reform nor diminish the total volume of crime.

Under the provisions of the Briggs law, enacted in 1924 in this state, the Department of Mental Diseases was authorized to examine all prisoners committed to jails for a period of thirty days or more or whenever there had been a previous sentence. A complete social service history is made in each case by a full-time social worker, and the psychiatric examination is then made by part time psychiatrists. The results of examination and recommendations are placed at the disposal of the Department of Correction. Over 8,000 persons have been examined, and the first 5,000 of these have been analyzed statistically: 91.5 per cent were male; 8.5 per cent were female. Further statistics relate only to male prisoners: 14 per cent were first offenders, but 49.5 per cent were serving their first commitment; about 8 per cent were under 20 years of age, 33 per cent between 20 and 30, 28 per cent between 30 and 40, and 30 per cent were over 40; of those under 30 years of age, the great majority were native born, and for the most part had been convicted of the more serious, aggressive offenses, such as breaking and entering, larceny and robbery; those older than 35, showed a greater percentage of foreign born; the native born white persons of native parentage formed 19 per cent of the group as compared with 30 per cent of the general population, according to the census; foreign born white persons in this study were 32 per cent, which was lower than the figure in the general population; the native born white people of foreign parentage total 31 per cent in this group, while the census shows only 20 per cent; in the group as a whole, 7 per cent never attended school, and an

additional 8 per cent discontinued school before the age of 12; less than 10 per cent attended high school. The unfortunate tendency of many schools to push children along regardless of their intellectual capacities has probably added to criminal tendencies of some of those who did go to school. In the early home life of criminals, up to the age of 17, poverty, intemperance, gross ignorance, immorality and broken homes are the rule, and only 14.4 per cent of the total group are listed as coming from good homes. A family history of recognized mental disease or deficiency appears in approximately 10 per cent of the cases.

Seventy per cent of the criminals in this group grew up under urban conditions. On the basis of religion, this study shows a classification almost identical with the figure of expectancy based on population. An exception occurs in criminals of Jewish religion, who constitute 2.7 per cent as compared with 6.7 per cent in the total population. Only 1.2 per cent are classified as drug addicts and 7.2 per cent as mentally defective; 3.2 per cent show actual psychoses. Alcoholic persons are concerned in 37.8 per cent of the cases. The always uncertain diagnosis of psychopathic personality is made in 15.5 per cent of cases, but rarely in persons over 35 years of age.

It is seen that the group is by no means homogeneous, and that segregation by classes would doubtless be advantageous. Gross inadequacy in regard to methods of dealing with drunkenness is revealed; perhaps this could best be handled by indeterminate commitment to special institutions. A similar disposition might be advantageous for psychopathic delinquents.

The services of the psychiatrist have been welcomed by all concerned in this study.

DISCUSSION OF PAPERS BY DR. OVERHOLSER AND DR. HOLT

DR. GUY G. FERNALD: This presentation is very illuminating and authoritative from the point of view of laboratory work. The relationship between the physician and the court is in a different sphere than the relationship between the defendant and the psychiatrist. I have enjoyed the professional assistance and conferences which these presentors have given me in the past.

DR. EDWARD B. LANE: I am much interested in Dr. Holt's paper. For some time I have been aware that the group of criminals has not received the care and treatment that it should have. I suppose that one cannot handle these people properly. What to do with the psychopathic woman who gets angry and even attempts to take her own life is a question. I think that such a person has not been given proper treatment. One can be as liberal and elastic as one pleases, but such a person should be confined.

DR. FREDERICK L. WELLS: I am impressed with the relation of the educational system to later conviction for crime. It has been noted before and has been impressed on us this evening that the criminal group escapes from the educational system much earlier than the normal. There is much more illiteracy and much less education. Does that indicate that the educational system guards against criminal careers? I look forward with interest to the contribution of these studies on this point.

DR. CHARLES A. MCDONALD: After the examination by the psychiatrist, what is his place in the court procedure? Does he testify? Has the defense a right to its own expert? In Rhode Island, there is no law like the Massachusetts law referred to, but by precedent, the court asks the state psychiatrist to examine the suspect; the defense may also have a psychiatrist, and the state may pay for both. After the examination carried on individually or collectively, the physicians consult and agree or disagree and then a third psychiatrist is appointed, medical consultation held, and a medical opinion given to the court. For several years there has not been a battle among the court psychiatrists—except when experts from other states have been called in. As to the second paper, I have enjoyed hearing the fine follow-up work that Massachusetts is doing. I am impressed by the

content of the paper: that his follow-up work is a social follow-up and not a psychiatric one. How long did it take to make the examinations in 4,500 cases and was the examination social or psychiatric; in other words, what does the presentor mean by psychiatric examination in this work?

DR. ABRAHAM MYERSON: I have had three connections with this type of work: (1) examination of prisoners under Dr. Holt at the jails in Norfolk, Middlesex and Suffolk; (2) work under the Briggs law, and (3) as psychiatric expert in court. I think that the psychiatrist makes his own place in the courts.

I regard crime as a social problem, only incidentally as a psychiatric one, unless the world belongs to the psychiatrist. The psychiatrist enters the scene in somewhat the spirit expressed by Menninger: "Since the law fails to take care of crime, let psychiatry take it over." Lawyers might well retort: since psychiatrists fail to stop insanity, let the lawyers take over these patients. The individual study is only a part of crime study. Cities afford a very unfavorable environment for criminals. The American born descendant of foreign born parents regards his parents as aliens, and therefore there is an emotional schism between the two groups. This expresses one phase of the relationship of culture and crime. An important question is the relationship between crime and political conditions. This, of course, is not psychiatric; it is cultural. The foreign born Italian is represented in murder statistics. His American born descendant commits robbery. This again shows the importance of culture in regard to crime. To define a criminal as a constitutional psychopathic inferior just because he is a chronic criminal is of no value in my opinion. From their histories, many persons fall into one category of personality type, not especially abnormal in intelligence. They belong to the unorganized extrovert. Intelligence, curiosity, industrial and sexual activities are unorganized. They "take things as they come and are not depressed." How shall we solve the crime problem? Reorganize society? Change our slums? Psychiatric attention to criminals is a very costly business.

DR. WINFRED OVERHOLSER: The right of the defendant to call witnesses to establish the fact that he is insane is a constitutional one and therefore cannot be taken away from him. Defendants rarely employ psychiatrists, however, in this state. The psychiatrists appointed by the Department of Mental Diseases are, of course, not infallible, but they are fair, impartial and competent. The defense usually recognizes this fact, and accepts their report. The procedure authorized by the Briggs' Law has been approved in two cases by the Supreme Court.

As for conferring, there is no reason why the psychiatrists retained by the two sides should not confer and every reason why they should. In a few cases, in fact, a psychiatrist retained by the defendant has been present with the department's examiners during their examination.

The legal profession, in spite of Dr. Myerson's somewhat pessimistic statement, is beginning to admit that the psychiatrist has something to contribute to the administration of criminal law. The American Bar Association for several years has had a committee on psychiatric jurisprudence, which has been in close touch with similar committees of the American Medical Association and the American Psychiatric Association. As a result of this recommendation, the American Bar Association has gone on record as favoring a mental examination before disposition in every felony case. The prejudices that have existed between the two professions are fortunately well on the way toward being broken down.

DR. EARL K. HOLT: The work of examining prisoners in the county institutions began in 1924. At that time, the Division for the Examination of Prisoners, Department of Mental Diseases, was organized, and the 5,000 cases included in the present survey represent examinations made during the first five years of the existence of the Division. The present organization is able to examine about 1,000 prisoners a year. In each case a thorough and searching investigation is made by a social worker before it is referred to a psychiatrist for the examination. The psychiatrist goes to the jail or house of correction, where the prisoner is serving a sentence, to make the examination. In answer to the specific inquiry of

Dr. McDonald as to the character of the examination, psychiatrists employed by the Division are representative men in this field, including such men as the president of this society, Dr. Myerson, and other men of recognized standing, and I have every reason to believe that the examinations are carefully done, and that they are both complete and competent.

Three Hundred and Ninety-Third Meeting, May 21, 1931

ABRAHAM MYERSON, M.D., *in the Chair*

ABNORMAL PERSONALITIES. DRS. WILLIAM HEALY, ERIC K. CLARKE and JACOB KASANIN.

From a summary of the literature, and especially of the extensive foreign literature, on abnormal personalities, it seems clear that the highly complicated classifications with various new terminologies proposed by foreign writers are not serviceable. Until the present research, most contributions have been based on considerations of the values of a certain schema rather than on the observation of a large number of cases with an attempt to ascertain what characteristics and careers have been displayed.

The first 5,000 cases at the Judge Baker Foundation have been reviewed carefully and all those that could properly be termed abnormal personalities have been studied by statistical workers, by psychiatrists who checked each other's opinions and by prolonged social service investigations to ascertain careers. Three hundred and thirty cases were found that properly belonged in the category of abnormal personalities. These were worked up statistically from the standpoint of characteristics displayed, and then classifications and definitions were considered. (The basis for these will be published in detail.) It stood out plainly that the "rag bag" classification so common in America, namely psychopathic personality, is totally inadequate. The German conception of constitutional inferiority is likewise limited in usefulness, and the French "déséquilibrés" and the English moral insanity are altogether unsatisfactory.

In this research, classifications and definitions were not developed theoretically nor as the result of preconceptions, but by directly facing the issues presented by the behavior and careers of individual patients. It was finally concluded that there are four discernible groups: *A*. The unstable egocentric personality is characterized chiefly by emotional instability and egocentricity, which actively and chronically thwarts achievement of the person's own aims and intended satisfactions that otherwise would be potentially attainable. In this group there were 120 cases; 72 males and 48 females.

B. The constitutionally inferior personality is characterized by habitual, inadequate behavior not accounted for by deficiency of intellectual endowment or by known physical disease. Nearly all such cases show definite signs of biologic inferiority. In this group were 100 cases; 83 males and 17 females.

C. The idiosyncratic personality (the odd or peculiar personality) shows in an otherwise normally integrated personality an abnormal predominance of one or more persistent characteristics that stand out clearly as marked deviations from the generally accepted norm. These characteristics are of various types and often do not thwart life goals and satisfactions. In this category there were ninety-eight cases; forty-six of the patients were males and fifty-two females.

D. The psychotoid personality shows behavior definitely resembling that of a typical psychosis (schizoid, paranoid, hypomanic, etc.), but in such a minor degree that the person cannot be considered psychotic. In this group there were 15 cases; 10 males and 5 females.

A control group of one hundred and twenty cases for comparison with group *A* was studied by the same methods. The careers of those in the various groups of abnormal personalities were shown to include many disasters; for example, seventy-two of the persons in group *A* who had been juvenile delinquents continued into careers of crime; thirty-one showed severe criminalistic behavior later on. In the control group, among the juvenile delinquents, a large proportion did well, very much better than those grouped under abnormal personalities, many of whom received a great deal of careful treatment, medical and social, and even placement under good environmental conditions.

A challenging example of the career of a young woman of fine mental ability, who showed through many years until death all the characteristics of group *A*, was given in illustration.

This research represents a step toward better understanding and better treatment in such cases, even though the fact is recognized that treatment often will demand permanent segregation of persons with certain types of abnormal personalities, especially those belonging to group *A*. Further medical and psychologic research is indicated if any therapy is ever to be effective.

DISCUSSION

DR. J. KASANIN: In regard to the statistical work, we had the classifications in mind before we approached the material. Statistics confirmed our previous ideas. The psychotoid group represents a group of children who have shown mild psychotic behavior. These have been followed for from eight to twelve years, and most of them have turned out well.

DR. C. M. CAMPBELL: This has been a most fascinating presentation of the field. Dr. Healy probably thinks that such a study requires the coordination of workers in many fields and not merely of a single group of specialists. A technic for further investigations must still be worked up. The study of the endocrine glands and of the nervous system will be of fundamental importance in any serious research into human personality.

DR. A. MYERSON: There is the question of the psychoanalytic examination.

DR. I. HENDRICK: The contributions to problems of this kind are considerable. Psychoanalysis might help answer questions as to why the girl whose case was reported did what she did. As to what psychoanalysts have accomplished in these cases, the most enthusiastic analyst would be somewhat modest by necessity. Psychoanalysis is rather new, and its chief material so far has been confined to psychoneuroses. The problem that confronts the psychoanalyst is that of undertaking a regimen in which the patient must play a most active rôle and take the initiative. First, there is the question of the possibility of being able to analyze. Second, there is the possibility, through training, of feeling justified in offering a theoretical interpretation. So far as what has actually been accomplished, an actual method of a modified psychoanalytic technic has been used by Aichorn. Alexander has not dealt sufficiently with this type of case, but with certain criminal types there are definite mechanics that have a very definite relation to psychoneurosis. The case that Dr. Healy has presented certainly gives some hints as to what is to be expected. Two very definite lines in the girl are characteristic: (1) her striving after something, not just impulsive outbreaks, but consistent seeking for something; (2) retribution, punishment, attempted suicide, etc., seem to be a general line in her development. One categorical statement may be made: In order to understand these aspects of her personality, one must know about her early life. If psychoanalytic technic should be successful, the patient would be able to reproduce the first five or six years of life; this is necessary to show the motives. This patient was not able, according to her own description in this beautiful letter, to find the motive. What these things would be, I think, are different from what Dr. Healy means by mechanics. The Oedipus complex is not a mechanism. It

is common to all human beings. It is not necessarily the Oedipus mechanism itself so much as the patient's particular reaction to the Oedipus complex that was this girl's heritage. Reich studied the formation of character and its relationship to this complex. The character formation is determined in that stage of development at which the greatest conflict develops and by the sex of the parent who caused it. I have in my own personal experience no actual material. I have had two cases in the last year that represent very definite egocentricities of character. One comes close to psychopathic personality, and the patient, a woman has shown definite improvement.

DR. M. R. KAUFMAN: Reich believed that psychoanalysts have a definite contribution, and he has analyzed psychopathic personalities with some success. Aichorn also arrived at the conclusion that these cases should be analyzed in institutions. Reich noted that some psychopathic personalities are akin to schizophrenia. A study of ten cases over a period of time by psychoanalysis might not only change the classification, but tell a little more about the psychopathic personality.

DR. A. MYERSON: I wish to ask three questions: 1. Is the outcome in these cases as hopeless as it seems to be when the study is limited to adolescence and early adult life? It is a common experience that men and women who get into trouble and display psychopathic traits undergo a spontaneous reformation and cure as they get older. In other words, before one reaches a pessimistic conclusion in regard to the various cases that Dr. Healy has presented, ought he not to know what happened to the subjects, how their lives were changed, how they passed out of their teens and twenty's into mature adult life?

2. Has it not also been shown, especially by Freeman, Holzinger and a group of Chicago men, that when children are placed out very early in life that they tend to resemble their foster-parents more than they do their real parents? In other words, it is of great importance to form character and to reform character very early. Dr. Healy and the others generally are first confronted by the social problem in such persons at the age of 13, 14, etc.; the prevention of the psychopathic personality types would seem to lie in making contact with the patients very early in their careers. The question is, therefore: Would not the prognosis and the general ability to handle these patients become greatly improved if access to them could be obtained very much earlier in their careers?

3. Do the psychopathic traits that these persons show explain their antisocial acts? Would one not find a huge amount of queerness of a similar type in the lives of men of genius, especially artists, literary men, rulers of nations and others?

The girl, whose case has been so interestingly presented, lacked a little of genius and had just a bit too much of vagrancy for a successful career. A little more genius and a little less vagrancy would have made her an interesting and socially valuable person.

DR. WILLIAM HEALY: Alexander wisely commented on the stereotyped behavior of egocentric persons. If this girl had also had a certain amount of functional stability, might she not have been able to use her talents? I would like to see ten cases worked out.

Dr. Kasanin did not invent the term psychotoid.

Dr. Gregg asks what could be done and what ought to be done in these cases. The cost of care runs up into hundreds of thousands of dollars, but this group of persons should be segregated, I think. One of our subjects was at Shirley and later he was in the army. He deserted from the navy twice. We have had quite a number of murderers. Colonization seems the only thing to do at present. Certainly, Dr. Myerson, the major wave of crime comes before 35. Then the subjects quiet down. As to the question of being with parents: Yes, children have been placed with foster parents, but the Chicago observers have not made studies of groups of this kind. We placed one boy out at 1 week of age and another at 2 weeks.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, April 24, 1931

DR. JOSEPH MCIVER, *President, in the Chair*

PRIMARY FIBROBLASTOMA OF THE BRAIN. DR. BERNARD J. ALPERS, DR. FRANCIS C. GRANT and DR. JOSEPH YASKIN.

A case of fibroblastoma, primary in the brain substance and unrelated to the meninges, was reported. The clinical course was rapid and fatal. Signs of increased pressure were not pronounced. The tumor was removed from the left precentral area. Histologically the growth was a typical fibroblastoma.

ALTERATION IN STRUCTURE OF SELLA TURCICA AS REVEALED BY THE X-RAYS. DR. KARL KORNBLUM.

This article will be published in full in a later issue of the ARCHIVES.

A CASE OF PARKINSONISM DUE TO MANGANESE POISONING. DR. HENRY F. PAGE and DR. C. A. PATTEN.

A man, aged 42, who had always been well, began working in a manganese plant in May, 1930. In September or October, 1930, he began to be drowsy and occasionally would fall asleep wherever he might be. He also became less interested in his children. Despite the symptoms he continued to work. In December, 1930, he complained of cramps in the muscles of the legs after unusual effort, more particularly after going to bed. Gradually speech and movements became slow and he noticed loss of grip in the hands. When walking he took very short steps and found difficulty in keeping from pitching forward when going down an incline. Two weeks before admission to the hospital he fell and injured himself slightly; this led to his leaving work and seeking medical advice. He continued to be sleepy and dull, had occasional frontal headache and lost all desire to exert himself. His appetite was enormous, but the bowels were costive.

On admission to the hospital on Feb. 4, 1931, he was in excellent nutrition, but presented a typical parkinsonian appearance and movement. The face was mask-like and the smile fixed; the forehead and upper lip were practically immobile. Some nystagmus was present on extreme lateral deviation of the eyes. Facial, lingual and palatal movements were extremely slow. Saliva accumulated in the mouth; the voice was husky and of low pitch, drawling and monotonous. The tongue had a coarse tremor. The extremities and trunk were stiff; the arms did not swing naturally in walking and there was a slight tendency to anteropulsion and retropulsion. All deep reflexes were overactive, but there was no clonus or Babinski sign. All other tests gave negative results.

General physical examination and laboratory tests yielded negative results. Many tests for manganese were made with the urine and feces, but all were negative. The blood was not agglutinated by the "Hammett" strain of Bacillus influenzae according to the method of Evans and Stewart for chronic encephalitis.

The diagnosis lay between postencephalitic parkinsonism and that due to manganese poisoning. In this case, in addition to working in manganese dust, the patient complained of severe cramps in the muscles of the legs.

DISCUSSION

DR. PATTEN: In reply to Dr. Trumper, calcium glucinate has not been used in this case. From a brief survey of the literature, it seems that persons suffering from manganese poisoning have been exposed to a dust containing more than 5 per cent for a period of not less than three months.

ANTAGONISTIC BIOCHEMICAL MECHANISMS IN DIABETES AND EPILEPSY. DR. MAX TRUMPER.

Years ago, observant clinicians noted some curious facts about immunity and spontaneous cure. One of the recent examples has been that infectious diseases, particularly those accompanied by high fever, sometimes cause the remission of symptoms in some forms of cerebrospinal syphilis. Many years passed before any one applied the mechanism present in high fever. It is now applied in the malarial treatment of dementia paralytica. This represents a disease that is antagonistic in effect to another disease, and in this case is applied as a therapeutic procedure in a second disease, namely, late syphilis. More recently, Loevenhart has demonstrated and Leake has confirmed the stimulating effects created by brief periods of inhalation of a mixture of 30 per cent carbon dioxide and oxygen, inducing mental clarity and intelligent responses in certain cases of catatonic dementia praecox. These favorable effects are only of from ten to fifteen minutes' duration.

Another group of phenomena involving intrinsic body mechanisms centers at the present time in the problem of epilepsy. The cause of idiopathic epilepsy is unknown. Many theories have been presented. The most promising trend at the present time is a physicochemical approach, involving such factors as distribution of ions, carbon dioxide, oxygen tension, water balance and acid-base equilibrium. The last factor has been used as a basis of a form of treatment from which satisfactory results have been reported. It rests on the observation and assumption that the development of a condition of relative acidosis reduces the frequency of the attacks. This state is brought about principally by the use of a ketogenic diet. It is known that for the complete combustion of 1.5 Gm. of fatty acid, 1 Gm. of dextrose is necessary. It is this ratio of fatty acid to dextrose that is termed the ketogenic antiketogenic ratio. When this ratio exceeds 1½, ketosis is apt to develop. In the ketogenic diet, carbohydrates are reduced to a minimum and fats increased with the view of increasing the hydrogen ion concentration of the body tissues and presumably of the sensitive brain tissue, the irritation of which occasions the attack.

These therapeutic measures aim to produce in the epileptic patient the very chemical condition that is found in the diabetic patient. Diabetes is associated with ketosis and anhydremia; epilepsy, on the contrary, is characterized by alkalosis and hydremia precipitating a seizure and is benefited by therapy designed to produce a state of ketosis and dehydration.

In epilepsy the observable symptomatology is so diversified and dramatic that its descriptive phenomena, which in reality are the result of some underlying condition, have received attention almost to the exclusion of the disease itself. There are many apparently diversified factors that have been reported clinically to be capable of initiating and modifying epileptic seizures. It has been found that seizures may be produced in susceptible persons by such measures as hyperventilation, by alkalosis produced by other means, such as the ingestion of excess alkalis and also by anoxemia.

Whenever a specific phenomenon can be produced by various measures that on the surface have little in common, there must exist a common denominator underlying these conditions. When one analyzes the various measures that are known to influence epileptic seizures both favorably and unfavorably, one finds that they revolve around one common chemical factor, namely, a disturbance of the acid-base equilibrium and its associated disturbance of the water balance. The disturbance of the acid-base equilibrium is fundamental in diabetes also, with a disturbance of the water balance as well. Low blood cholesterol values are found in epileptic seizures in contrast to high cholesterol values in diabetic patients who are dehydrated and doing poorly.

Both high and low blood sugar values have been reported in epileptic seizures. This at first may seem at variance with my concept of diabetes verus epilepsy. But it is a known physiologic fact that in the presence of an adequate glycogen reserve

in the liver convulsive seizures result in hyperglycemia due to increased hepatic glycogenolysis. In convulsive seizures, when the glycogen reserve of the liver is inadequate, low blood sugar values are found. Thus the blood sugar values in epilepsy depend on the state of carbohydrate nutrition at the time the specimens of blood are obtained.

In epilepsy and diabetes the fundamental chemical mechanisms are, in part at least, antagonistic. Therefore, from this point of view, theoretically the incidence of epilepsy in diabetes should be extremely rare because the ketosis and dehydration that are prominent features of diabetes constitute a mechanism that is in direct antagonism to the underlying features of epilepsy. Clinical experience appears to confirm my theoretical observation. Professor Joslin, in a recent personal communication, has stated: "At present, among about 8,500 cases of true diabetes, there are 10 cases of epilepsy and 3 cases that are possibly epileptic." Dr. S. F. Adams of the Mayo Clinic wrote me as follows: "The incidence of epilepsy in our diabetic patients has been very small. Without looking through our files I would venture to guess that in the last ten years we have not had more than 10 cases of epilepsy in about 3,000 cases of diabetes." From the diabetic clinic of the Grace Hospital in Detroit, Drs. Wendt and Peck reported no epilepsy in 1,073 cases of diabetes. Dr. Rabinowitch of Montreal has written me of only 2 epileptic patients from their large diabetic clinic. Thus, in a total of approximately 15,000 diabetic patients, there have been at most but 25 cases of epilepsy.

If an epileptic patient is known to have diabetes, one must be guarded in the use of a ketogenic diet for the control of the epilepsy. Dr. F. B. Talbot, in his recent book on the use of the ketogenic diet, said that "patients who follow the diet carefully and maintain it from four to six months often are gradually able to shift back to a normal diet and still be free from epileptic seizures. Occasionally relapses may be expected." He did not, I believe, offer any explanation. However, on the basis of my studies on hematorespiratory compensation, I believe the fact to be due to the fixed type of breathing of these patients, in place of the irregular and unstable breathing ordinarily found in the epileptic patient. One must be careful in treating the epileptic patient who has diabetes, because an artificial ketosis will be superimposed on the already existing state of ketosis and will cause the associated dehydration to become extreme enough to induce convulsions.

In conclusion, I wish to emphasize the need for careful study as well as for conservative treatment of that unusual patient who presents both conditions. During the past decade very few of the children with diabetes survived, and this may account for the scarcity of patients having both diabetes and epilepsy. Or the scarcity may be due to the antagonistic effect of diabetes on epilepsy. A study of such cases should give a clearer insight into the causation and control of epilepsy.

Osteitis Fibrosa Cystica of the Skull Associated with Hemianopic and Psychotic Symptoms. Dr. Harold D. Palmer.

This article is to be published elsewhere.

A New Apparatus for Replacement of Cerebrospinal Fluid by Air in Encephalography and Ventriculography. Dr. F. C. Sommer.

The procedure of ventriculography is not without considerable danger even in the most experienced hands. It carries with it a risk of life too great for a diagnostic method. The mortality has been variously found to lie between 8 per cent by Grant (Arch. Neurol. & Psychiat. **14**:513 [Oct.] 1925) and 12 per cent by Rosenheck (Arch. Neurol. & Psychiat. **22**:575 [Sept.] 1929). On the other hand, encephalography is decidedly safer, resulting in only 0.67 per cent deaths in a series of 895 consecutive operations reported by Bingel (*Klin. Wchnschr.* **7**:2336 [Dec.] 1928). In attempting to perfect a method by which the mortality rate for ventriculography may be lowered, it is necessary to emphasize the factors responsible for the majority of deaths and to estimate their relative importance as

the cause of mortality. As the procedure has been carried out, these factors are generally conceded to be three: 1. The needle must pierce brain tissue and possibly tear blood vessels. These are unavoidable occurrences, but death attributable to them is rare. 2. The air itself may cause irritation, with a resulting meningitic syndrome. This also cannot be avoided, but if it were an active factor, one would expect more frequent disturbances to follow injection of air by the lumbar route. 3. Marked fluctuations of intracranial pressure occur during the procedure, with attendant displacement of the pathologic mass and direct and remote pressure effects on the brain itself. This last factor cannot easily be obviated by any of the methods previously in use. It is incidentally, the one responsible for most of the mortality resulting from the procedure, as I shall show.

Following ventriculography, it has been found that the majority of deaths occur: (1) in patients with large intracranial lesions, irrespective of their location, (2) in

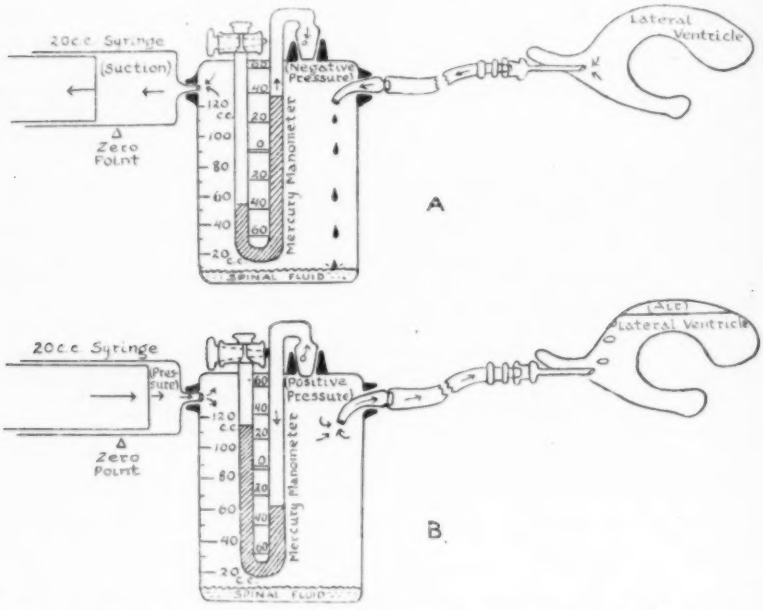

Fig. 1.—Diagram showing the apparatus. *A* illustrates the withdrawal of fluid. The fluid displaces an equal amount of air from the bottle into the syringe. *B* illustrates the return of that amount of air to the ventricle. An accurate reading of the intracranial pressure is obtainable at any time by pressing forward the syringe barrel until the flow of fluid comes to a standstill as indicated by the stationary bubble in the dropping nozzle.

ventricular blocks, and (3) in conditions associated with high intracranial pressure. The mechanism of the immediate cause of death in these cases is hemorrhage from the poorly supported and often diseased blood vessels of a large tumor or abscess, hernia of the medulla into the foramen magnum or development of acute cerebral edema. Such occurrences can nearly always be explained on the basis of increased or decreased intracranial pressure during the operation. If the pressure is changed within the ventricles, the size and shape of their collapsible walls must change accordingly, and this distortion and displacement of brain tissue and the pathologic mass directly cause damage to the vascular system or produce acute cerebral edema.

Then again, even though the fluctuations of pressure in a given patient are not sufficient to cause death, they frequently excite severe headache which is difficult to

relieve. As evidence that it is not alone the presence of air in the subarachnoid and ventricular spaces that causes the headache, I report the cases of the first eight patients on whom the apparatus was used. This group included four cases of brain tumor and one of diffuse cerebral sclerosis. All patients were mentally clear. Only one complained of headache, and this for only a few hours following the procedure. Furthermore, every one is familiar with the intense headache that frequently follows a routine spinal tap with the removal of 10 cc. of fluid. This most certainly is a result of disturbed pressure.

It can be assumed, then, that if the fluid could be replaced by air without any appreciable change in intraventricular contour or pressure, mortality and morbidity would be correspondingly decreased. To accomplish this desired maintenance of pressure, I have designed an apparatus that will permit the exchange with a variation in pressure of only a few millimeters of mercury. It also possesses definite advantages over other instruments and methods in accuracy, simplicity, ease of manipulation and speed with which it is operated.

The encephalometer consists of four detachable parts: a pyrex glass bottle, of 130 cc. capacity, with self-retaining friction attachments as the remaining three parts, viz., a 20 cc. syringe, a mercury manometer and a rubber tubing connection

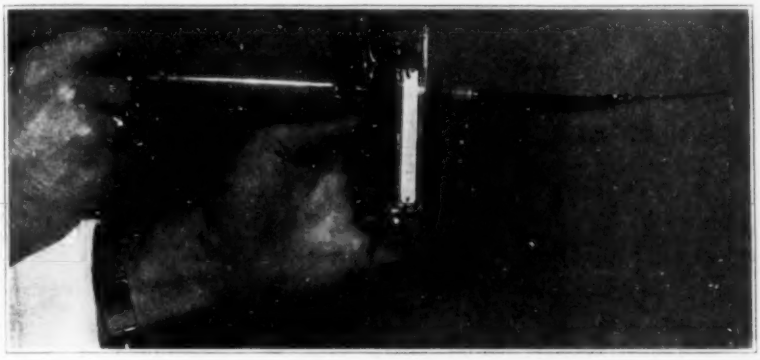

Fig. 2.—Photograph of the apparatus, showing the method of manipulation.

to the tap needle. The whole apparatus is clearly shown in the accompanying diagram. It can be sterilized by boiling.

Technic for Use of Encephalometer.—Several physical principles applying to the construction of the apparatus must be kept in mind in order to understand its operation.

1. The apparatus is entirely closed, but its pressure can be varied, plus or minus, by the attached 20 cc. syringe. When the apparatus is connected to the already inserted needle its pressure is zero, while that of the ventricles is plus 6 or more. Because of this difference in pressure, fluid flows into the apparatus at its original pressure, minus that which is lost in overcoming friction in its passage through the tube and needle. If the syringe barrel is pressed on, the pressure in the bottle thus being raised to the point at which the stream of fluid comes to a standstill, the pressure in the bottle equals that of the ventricles, and the attached manometer registers that pressure. (Friction plays no part in the reading while the fluid is motionless in the connecting tube.) The point to which the syringe must be forced in order to bring the flow of fluid to a standstill is noted and taken as the zero point. When the syringe barrel is pressed farther, air is forced into the ventricles; when it is withdrawn to the other side of the mark, fluid flows into the apparatus

from the ventricles. If the syringe barrel is returned to this position after each small removal of fluid and replacement of air, the intraventricular pressure must remain constant through the operation. It is obvious that the rather appalling fluctuations in the manometer readings during rapid withdrawal of fluid and injection of air can be disregarded, as this reading represents intracranial pressure plus the amount of force necessary to overcome resistance in the passage of fluid through the tube and needle at a given rate.

2. Again, because the apparatus is closed, only the amount of air displaced into the syringe by the fluid that enters the bottle can be returned to the ventricles. This statement must be qualified, however. With the apparatus in operation there is always an extra distance that the syringe must be closed beyond the zero point in order to start the air into the ventricles. This distance, transformed to terms of pressure, represents the force that must be used to overcome friction of the residual fluid (1 cc. in amount) in the tube in front of the column of air to be injected. When the fluid is expelled and the air reaches the needle point, the resistance is suddenly diminished, and air rushes rapidly into the ventricle. This amount of air exceeds the amount of fluid already withdrawn if the force is not immediately taken off the syringe and the barrel allowed to slide back to the zero point, at which the proper amount of exchange is completed. This is the only precaution that must be observed so that the air volume will be exactly equal to the amount of fluid withdrawn.

3. It is often advisable to inject a little less air than the amount of fluid withdrawn to allow for expansion of air at body temperature compared to that at room temperature. This amount is approximately three one hundredths times the volume injected for a change from 80 to 98.4 F., or about 1 cc. less air for every 33 cc. of fluid withdrawn. However, this slight variation need scarcely be accounted for, unless large amounts of fluid are to be replaced.

4. Fluctuation of intraventricular pressure is dependent on the amount of fluid withdrawn from the ventricle each time rather than on the rate at which this is done. In practice, 3 cc. of fluid withdrawn from the ventricles scarcely changes its pressure, unless the ventricle is blocked and extremely small and inelastic. It is possible then to withdraw fluid and replace it with air as rapidly as desired without doing damage if small amounts are exchanged. This can be accomplished in about half of the time required by other methods, as there is no stopcock to turn or syringe to be detached between withdrawal or injection.

After these preliminary considerations of volume, pressure and resistance as applied to the apparatus and ventricular system, I can proceed with a description of the use of the instrument.

The patient is arranged, prepared and draped as desired. The needle is inserted either in the lumbar region or through a small occipital trephine opening. The apparatus is equally efficient by either method. A plain Luer or stopcock needle of about twenty gage size should be employed. In encephalography it will be found that a more complete and rapid exchange of fluid for air is made possible by performing the operation with the patient lying on an operating table inclined from head to foot at an angle of about 20 degrees. In this position air locks in the spinal subarachnoid space are avoided, since the air tends to rise cephalward along the upper side of the spinal cord and the fluid descends at the same time along the dependent side of the cord. The necessary manipulations of the patient's head can also be carried out to better advantage.

The assembled and sterilized apparatus is adjusted with the 20 cc. syringe withdrawn to the 10 cc. mark, and the manometer valves open. It is then attached to the already inserted needle. When fluid begins to enter the bottle from the dropping nozzle the syringe barrel is pressed on, the pressure in the bottle thus being raised, until the fluid ceases to flow, as shown by the stationary bubble in the glass nozzle. The manometer reading then represents intracranial pressure, since the pressure in the bottle must equal that of the ventricle, or the fluid would

flow one way or the other in the tube. It is most important at this point to note the position of the syringe barrel; it will lie somewhere between the 10 cc. and the 1 cc. marks, depending on the height of intracranial pressure. This position of the barrel at which the pressure in the apparatus equals that of the ventricle can be designated as the zero point. To proceed with the exchange of air for fluid, the syringe barrel is drawn on, which produces negative pressure in the bottle. Fluid enters from the dropping nozzle. Only about 2 or 3 cc. is taken. To replace that amount with air the syringe barrel is pressed forward, which raises the pressure within the apparatus and drives the residual fluid in the tube and needle ahead of the column of air into the ventricle. The resistance of the fluid left in the tube requires that more pressure be exerted to drive it back into the ventricle than that of the intraventricular pressure. Hence, the syringe must be closed a certain distance beyond the previously determined zero point. But when the fluid leaves the tube and needle the friction of the air passing through amounts to practically nothing; the extra pressure is no longer needed, and must be removed or more air will enter the ventricle than there was fluid withdrawn. This is accomplished by bringing the syringe barrel back to the zero point when the manometer column begins to fall. The complete exchange is carried out by a repetition of alternate withdrawals of fluid and injections of air in the manner described.

This rather protracted description of the technic of manipulation of the instrument might give one the impression that the procedure is a complicated one. However, this is not the case, as a brief examination of the apparatus during its operation will show.

The only error that can easily be made is that of returning too much air to the ventricles. This does not prove to be a very damaging mistake, as the extra amount cannot exceed a total of more than 3 or 4 cc. for the whole procedure. Its occurrence is made obvious at any time by taking a manometer reading, as directed at the beginning of the operation.

The physical principles involved can be proved to be correct in their application by tying off the cuff of a rubber glove filled with water and inserting two needles. To one needle is attached a standard mercury manometer, and to the other the encephalometer. By proceeding as previously described, the glove can be quickly emptied of water and filled with air, its pressure at no time varying more than 1 or 2 mm. of mercury. This is also a valuable method of mastering the technic of the procedure.

Features of practical importance in the use of such an instrument are: 1. The apparatus is compact and easy of manipulation without assistance. 2. Only one needle is inserted. 3. Displacement of the needle during manipulation is avoided by the interposed pliable rubber tubing. 4. The apparatus is applicable and safe in all cases. There is a sense of security on the part of the surgeon in knowing that during the procedure the ventricles must maintain their original contour and pressure. 5. The entire apparatus can be sterilized by boiling, and set up for use assembled. 6. The possibility of infection is at a minimum, since after the original attachment to the needle there is no other contact with the lumen of the apparatus. 7. The procedure can be interrupted at any time by clamping the rubber tubing with a hemostat and disconnecting the bottle. This is necessary when more than 130 cc. of fluid is to be replaced. After emptying the bottle, the operation is resumed in the same manner as it was started. 8. After the x-ray films have been taken, the air in the ventricles can be largely removed, and the sterile spinal fluid, which has been left in the apparatus, returned in equal amounts. This is accomplished by reinserting the needle, reversing the position of the patient and proceeding as before, but with the apparatus turned upside down.

Summary.—Believing that variation of intracranial pressure during the replacement of spinal fluid by air in ventriculography is the principal cause of the high mortality accompanying this procedure, I have devised an apparatus that will permit

this exchange without appreciable deviation of pressure, or alteration of ventricular contour, throughout the procedure. In addition it is practical in use, combining the requisites of simplicity, rapidity and safety of operation.

The apparatus is manufactured by the George P. Pilling and Son Co., Philadelphia.

DISCUSSION

DR. F. C. GRANT: I have had no experience with this apparatus, but it seems worth while. Certainly, if one can keep the intracranial pressure at the same level during the operative procedure I am sure that it will reduce the mortality from ventriculography. Dr. Sommer used my name in citing 8 per cent mortality. I wish to lay that ghost if possible. These figures were given four or five years ago; they were taken in a collective survey by twenty-five or thirty men. The number is too high. I know that our present mortality is less than 5 per cent. Furthermore, the comparison of mortality in encephalography to that in ventriculography comes up. It is unfair to compare these cases. Of the ventriculographies included in the original report, only 15 per cent were done in cases without brain tumors. Brain tumor is a condition entirely different from those in which encephalography is usually done. Encephalography is being performed now in almost every circumstance. It is unfair to compare the introduction of air in these cases in which brain tumor was frequent with others. Furthermore, between 35 and 40 per cent mortality occurs among patients with brain tumor. The cases from which the figures are secured are the type of cases in which ventriculographies are done. It is unfair to compare these conditions with those in which encephalographies are performed. There is one other point that is important. Neurosurgical clinics have cut down the mortality in these cases by operating as soon as a diagnosis is made. If air is introduced into a brain, a roentgenogram is made in half an hour and operation performed as soon as possible after that. The patients do not die from encephalography, they die because of the operation. Air sets up an irritation. If there is an intracranial mass or pressure present, and added to this is an intracranial lesion or mass, the condition will be serious. If the instrument described will keep pressure at a certain level it will be valuable. I believe that to get satisfactory ventriculograms one must remove all the fluid before putting in air. Whether that can be done with this apparatus is questionable. The cases in which diagnoses are made from encephalograms or ventriculograms are cases in which one can withdraw all the fluid and insert air.

DR. T. A. SHALLOW: This apparatus is practically a bi-pas syringe. One starts with 5 cm. of pressure and, of course, the amount of air that is in the reservoir. The apparatus will reverse itself practically to the position from which it was originally taken. One can increase the amount of air in the reservoir. I shall say in passing that Dr. Grant is entirely right about leaving air in the ventricles. The proper procedure is to make preparations the day before, be prepared to take a ventriculogram in the morning; take the roentgenogram at 10 a. m., have it read at 11 and operate at 12. One should not wait two or three days for an interpretation of the roentgenogram. The mortality from the procedure can certainly be cut down in this manner.

Regular Meeting, May 22, 1931

JOSEPH MCIVER, M.D., *President, in the Chair*

TUMOR OF THE PARIETAL LOBE. DR. ALEX SILVERSTEIN.

This case is reported because of its unusually interesting symptomatology and the apparently close relationship between the clinical neurologic signs and the anatomic-physiologic processes in a patient with a progressive brain lesion. Furthermore, it serves as additional proof for the contention that cerebral muscular

atrophy is due to an involvement of the parietal lobe. The case is also interesting in view of the modern tendency among physiologists to question accurate cortical localization.

History.—A. V., a man, aged 42, a drug salesman, was referred by Dr. D. J. Donnelly on Nov. 29, 1930, complaining of twitching of the left side of the face and thickness of speech. The past medical history was unimportant except for an empyema in 1900. The family history was without significance with one exception: the father of the patient died of cancer of the throat.

The patient had been well until five weeks prior to coming under observation, when he noticed that on two or more occasions his tongue interfered with speech by "getting in his way." Two weeks later, he had an attack in which the left half of the tongue, the floor of the mouth and the left half of the face became cold. Simultaneously, the tongue felt as if it were curled up in the mouth. This was immediately followed by a severe spasm of the left side of the face. The attack lasted about one minute and was not associated with loss of consciousness. He was free from symptoms until a similar attack on Nov. 21, 1931, when he was referred for study.

No positive neurologic signs were detected at this time other than a slight ironing out of the lower left side of the face, although he was able to pull up the corners of the mouth equally well on both sides. The speech was thick with a tendency to slurring. The reflexes in the upper extremities were equal. Dynamometer readings were: right hand, 90, and left hand, 85. The patellar and ankle jerks were prompt on both sides. There were no cerebellar or sensory disturbances.

Following a severe attack of twitching of the face, the patient was admitted to the Temple University Hospital on Dec. 17, 1930, where the following seizures were observed: He ceased talking because of a feeling of constriction in the throat and "tremulous jerks in the Adam's apple." At the same time there were numbness and a cold sensation of the left half of the tongue, of the floor of the mouth and especially of the inner side of the cheek on the left side of the face, followed by slow twitchings of the platysma muscle, increasing in intensity, frequency and severity, which resulted in powerful contractions of the muscles of the left side of the face, excluding the eyes and forehead. These attacks would last about one minute and were not associated with loss of consciousness. They varied from a numbness of the left half of the tongue with a few twitchings of the muscles to severe contractions. The patient would have as many as thirty-three spells a day, which seemed to be precipitated by movements of the head to either side and forward, but less when the head was bent backward. During the interval between seizures, the left half of the tongue and inner side of the left cheek would feel like "effervescent salt or gravel."

Neurologic Examination.—The olfactory sense was preserved on both sides. The fundi were normal. The pupils were 3 mm. in diameter, and responded promptly to light and in accommodation. The third, fourth and sixth cranial nerves were normal. The corneal and conjunctival reflexes were active on both sides. There were a Horner syndrome on the right and an ironing out of the left lower part of the face, and in drawing up the corners of the mouth there was an exhaustibility of the muscles on the left side. Hearing was good in both ears. Speech showed marked changes during the spells of constriction in the throat. The dynamometer readings were: left hand, 85, and right hand, 95, as at the previous examination. The senses of vibration, position, touch, passive motion and difference in weights were all normal. The patient was able to recognize immediately the difference in the textures of fabrics, such as silk, cotton and wool. Taste sensation was preserved on the anterior and posterior aspects of the tongue. The tongue had a tremor simulating fibrillation, and was slightly atrophic. The palate on the left side was slightly lower than on the right.

Miscellaneous Studies.—Urinalysis and examination of the blood gave negative results. The spinal fluid pressure was 8 mm. of mercury. Wassermann reactions

of the blood and spinal fluid were negative. Roentgen examination of the skull showed a normal appearance. The encephalogram report by Dr. Chamberlain was as follows: "The subarachnoid channels were completely absent from a sharply localized area over the vault, immediately to the right of the sagittal suture. The right cerebral ventricle was completely visualized and was slightly displaced to the left side. The left lateral ventricle did not contain any air." Bárány tests by Dr. Julius Winston showed: The response from the left horizontal semicircular canal was perverted. Hearing was good in both ears. These observations indicated the presence of an intracranial lesion. A lesion in the right temporoparietal region was suspected. Examination of the vocal chords by Dr. Chevalier Jackson revealed: "At the time of examination the laryngeal motility was perfectly normal, including the tension."

Course in the Hospital.—The neurologic signs remained practically the same. On Jan. 3, 1931, there was evidence of slight atrophy of the left hand, especially at the region of the first dorsal interossei, without any weakness or sensory disturbances. The left patellar reflex was slightly more prompt than the right. The patient was discharged from the hospital on the following day with a diagnosis of a tumor of the brain in the right parietal region, low down, extending anteriorly to the third frontal convolution.

Subsequent Course.—The condition was watched for progression of the atrophy in the left upper extremity and the appearance of paresthesia of the thumb and index finger. On January 21, while in Dr. Donnelly's office, the patient had the following spell: The voice weakened until he was unable to utter a sound. The left side of the face from the angle of the mouth up to the zygoma felt numb and cold, involving at the same time the thumb and index fingers of the left hand, which seemed to "go to sleep." He had to shake the left hand forcibly before a normal feeling returned. The attack lasted about five minutes.

On January 23, examination revealed the following additional neurologic signs: There were nystagmoid movements when looking laterally, especially to the left; there was a marked increase in the facial weakness on the left side; the soft palate was in a state of continual jerking, suggesting an epilepsia partialis continua; the atrophy of the tongue and left upper extremity was more marked; tests for sensation and reflexes gave negative results, as on previous examinations. During one of the spells, which was observed at the examination, the tongue and soft palate partook of the same forceful contractions as the facial muscles.

On February 17, the patient reported that he had had many more spells consisting of numbness of the face, thumb and index fingers, and that he had also had an attack that involved the thumb and index fingers in both hands. He had had sensations of coldness extending from the wrist down. In another attack the paresthesia started with a loss of feeling in the left thumb and gradually passed over the other fingers up to the left upper extremity. He also reported that occasionally a severe attack of jerkings of the left side of the face involved the forehead of the opposite side of the face. At this examination the neurologic signs showed a distinct increase in the atrophy of the left hand. The measurements of the biceps, 1½ inches (3.8 cm.) above the elbow, were: right, 9 (22.86 cm.), and left, 8½ inches (21 cm.). The whole left upper extremity was paler, colder and more delicate than the right. The overlying skin was smooth and glossy. The muscles were soft and flabby, with loss of tone, which seemed to have melted away. The grip in both hands was normal. For the first time there were slight sensory changes. The patient was unable to recognize slight changes in the position of the fingers of the left hand. However, stereognosis, graphesthesia and tactile sensations were all normal. There was hypesthesia of the left side of the face and the radial side of the hand.

Readmission.—On February 26, the patient was readmitted to the Temple University Hospital on the neurologic service of Dr. Winkelman. Examination revealed the following positive signs: There was a definitely marked left central

facial palsy, noticed even on emotional display, and accentuated by the fact that there was a Horner syndrome on the right. The tongue was extremely fibrillary and atrophic. The uvula was also atrophic on the left side, but was moved upward in the median line. The corneal reflexes were both present, but the right seemed a little more sensitive. There was a marked difference in the perception of pain in the face on the two sides; it was perceived more acutely on the right and produced a muscular contraction. There was a flaccid paralysis of the left upper limb with considerable atrophy, particularly notable from the wrist down. The left biceps reflex was hyperactive, and the left patellar reflex was also more prompt. On stroking the soles of both feet there was an upward extension of the toes on both sides, but this was apparently a defense movement. There was definite astereognosis and loss of sense of position of the fingers in the left hand.

The summary of an ocular examination on March 3, by Dr. Sloane, showed a beginning papillitis in the right eye. The fields were normal.

The condition of the patient became progressively worse; the left hemiplegia became more marked, and the reflexes in the upper and lower extremities of that side were markedly diminished.

Operation.—On March 6, Dr. Temple Fay reported the operation as follows: The bone flap was designed so as to make its center over the rolandic area, exposing the frontal and parietal lobes. On opening the bone flap, the dura was very vascular. The dura was opened with the flap toward the vertex, immediately disclosing a glassy-red, tumor-like cortex, extending from the sylvian fissure half way to the vertex and lying between the rolandic fissure and postcentral convolution. The tumor was firm and cartilaginous. In the lower posterior third there appeared to be a granulomatous cortex rather than a separate tumor mass. The involved area was isolated by the electrocautery; dissection was carried down to a depth of 3 cm., when soft yellow brain tissue was encountered. Finger dissection freed the tumor mass from its deep structure.

Pathologic Examination.—Dr. N. Winkelman reported a structure characteristic of the spongioblastoma multiforme type of glioma.

Postoperative Course.—This was surprisingly satisfactory considering the type of lesion. The patient progressed favorably from day to day. The power in the left limb was first to return. On March 17, eleven days after the operation, he was able to make a fist and to raise and lower the upper limb. The wasting seemed to be more intense in the left upper extremity, and some atrophy was evident in the left half of the face. The paralysis of the face was slightly improved, and the left side of the face moved on emotional display. The electrical reactions, taken on March 24, showed a quantitative loss both to galvanic and faradic stimuli, but there were no reactions of degeneration. The sensory disturbances gradually diminished. There was little evidence of astereognosis, as the patient was able to recognize different textures, size of coins, gross objects, such as a key, etc. The sense of position and passive motion of the fingers of the left hand showed a disturbance only to a slight degree as compared with the opposite side. The patient was discharged from the hospital on April 19.

On May 19, the patient stated that for the past few days he had noticed a "small area of coolness," about 1 inch (1.3 cm.) in size, usually in the left upper corner of the mouth, although such areas had occurred in all parts of the left side of the face and on the left hand. He could wrinkle the forehead on the left but not on the right or uninvolved side. There was more power in the left upper extremity. The dynamometer reading indicated: left hand, 20, and right hand, 75. Sensation was practically normal. The wasting was still marked on the left side and also to a much lesser degree on the right.

Comment.—A number of features are of anatomic and physiologic interest:

1. The interesting association of jacksonian, sensory and motor seizures, involving the pharynx, larynx, tongue and face, followed later by the evidence of slight weakness of the muscles of the left side of the face, prompted the visualization

of a pathologic process extending from the lowermost portion of the postcentral gyrus bordering the fissure of sylvius and posterior to the rolandic fissure. The spreading of the disease process upward and outward into the parietal lobe would anatomically involve, in order, the thumb and index fingers in the form of paresthesias, and if our contentions on the trophic functions of the parietal lobe are correct, atrophy in the extremities should have resulted, which later proved to be precisely as we had anticipated.

2. There was progressive increase in the paralysis of the left side of the face, until it resembled a peripheral palsy with a complete loss of voluntary and emotional responses, and there was a return of the latter function following operation. The recent weakness of the muscles of the right side of the forehead, a site that was occasionally involved in the spreading of the jacksonian motor seizures from the left lower part of the face, is of interest but difficult to explain.

3. The disappearance of the epilepsia partialis continua of the soft palate, together with the other jacksonian motor and sensory seizures, at the onset of the hemiplegia is certainly suggestive of a destruction of the gray matter with an extension of the pathologic process into the subcortex.

4. The typical spreading of the sensory jacksonian fits, with the radicular distribution to the thumb and index fingers, is in harmony with the result of the researches of Cushing and van Valkenburg, who found by electrically stimulating the postcentral gyrus in conscious patients that the sensory centers in this region were closely analogous to those of the motor points in the precentral gyrus. The paresthesias of numbness, "falling asleep" and "choking sensation" which these authors produced are similar to those in our case. Besides this anatomic progression of the paresthesia, the response of which is thought to be due to a weak stimulus, there are numerous combinations of sensory loss possible from cortical lesions. This subject has been treated by Head, Goidstein, Sittig, Spiller, Foerster and others.

The occurrence of jacksonian fits involving simultaneously both extremities, as was present in our patient, is an extremely rare observation in a human being and is questioned by many. The conclusions of Dusser DeBarenne on animals must be referred to here. He found that, immediately after applying strychnine to a small area of the cortex, various symptoms appeared on the corresponding parts of the two sides of the body, such as hyperesthesia, but more on the side opposite to the site of stimulation. Although his experiments show a possibility of a bilateral sensory disturbance from a unilateral cortical lesion in animals, this has not been found to be true clinically. The first clinical analogy to Barenne's observations was in a case of Potzl, who reported the case of a patient with an abscess in the frontal lobe, seen at operation, which produced paresthesia simultaneously of the right hand and forearm and sometimes spread to the left arm. At other times the paresthesias passed from the left arm to the right leg. There was no autopsy in this case.

It is to be noted that most of the cases discussed by Spiller and others on sensory jacksonian seizures, whether associated with or without motor fits, were located in the parietal lobe.

5. The last and most important feature of the case herein reported is the early appearance of atrophy in the left upper extremity, which, as in a similar case described by Burr, in 1902, seemed like "a true melting away of muscle fibres." This was especially significant, as we could find no evidence of any motor disturbances and only mild sensory changes, such as the inability to recognize slight differences in the position of the fingers without astereognosis. The atrophy of the uvula and the tongue, together with the speech and swallowing difficulties, strongly suggested a bulbar involvement, but can be understood because of the low site of the lesion in the postrolandic area. We have not seen atrophy of the tongue in any of our other cases of parietal lobe lesions. Spiller described a case of marked unilateral atrophy of the tongue in a patient with infantile cerebral hemiplegia. In our case the wasting was on both sides of the tongue.

At this time it is interesting to mention a case reported by Morton Prince before the American Neurological Association in 1906. He described a patient who had attacks of jacksonian sensory and motor seizures with early marked wasting of the upper extremity, and in whom flaccid hemiplegia and sensory changes with marked increase in the atrophy developed progressively. The tumor was located primarily posterior to the fissure of Rolando, centralized in the post-central convolution and extended backward to the parietal lobe and forward into the anterior central convolution. This case is similar to the case herein reported.

Time does not permit a discussion of central atrophy in brain tumor. However, I shall emphasize that we have proof that the parietal lobe contains a specialized group of cells which from clinicopathologic evidence we can state is in the posterior part of the postcentral gyrus, which is architecturally different from the anterior part of the gyrus. This location explains the almost constant association of the atrophy with sensory changes, as astereognosis and the like, in our cases of parietal lobe tumors. Bearing in mind the close proximity of the trophic region to the superior parietal lobe, an area Mills and Weisenberg presented in 1907 as the stereognostic center, it was gratifying to read of the following case of tumor of the superior parietal lobe reported by Mills, Keene and Spiller (1900). The progressive atrophy in the extremities was so striking as to warrant a special study of this phenomenon by Mills, in association with Spiller, Osler and Lloyd. Mills concluded that "certain regions of the cerebrum may induce atrophy by acting from a distance on the lower spinal centers." These cerebral trophic centers are probably not to be sought in the motor region of the motor cortex, as has been suggested by some observers, but in the limbic and parietal lobe. It was a tremendous satisfaction to learn that our conclusions as to the significance of central atrophy, which we believe to be due to a parietal lobe involvement, had been propounded by Charles K. Mills.

DISCUSSION

DR. N. W. WINKELMAN: There was some doubt at first as to whether this patient had a bulbar palsy, because of the peculiar symptomatology. I have been interested in the type of cortical atrophy observed in this patient. Personally, I can palpate the atrophy before I can see it. There is, in addition, a change in the texture of the overlying skin. Seldom do I have to resort to measurement. It may be that the entire picture is of vasomotor origin. I am convinced that there is an area in the parietal lobe adjacent to the motor area that has to do with trophic influence on the muscle and overlying tissue; I believe also that it is rarely involved alone, because of the proximity of the motor cortex.

A great part, if not all, of the lesion was removed at the operation, and while this is a very malignant type of glioma, the operation has had the effect of giving the patient many additional months of life. It was interesting to see the tumor actually grow under our eyes in the course of days, not weeks; the physiology of the cortex was displayed before us.

DR. J. C. YASKIN: How does Dr. Silverstein account for the Horner syndrome which in this case he seems to have regarded as an early sign of parietal lobe tumor? He also mentions the appearance of a rather persistent nystagmoid movement. Particularly interesting would be an explanation of the Horner syndrome in the case of the parietal lobe tumor.

DR. W. G. SPILLER: While I assent largely to what has been said regarding the importance of the parietal lobe in the production of cerebral atrophy, I am not convinced that the motor cortex has no part in this form of atrophy. If the portion of the brain recognized as the recipient of afferent sensory impulses, viz., the parietal lobe, is the only part of the cerebrum having influence over the trophic condition of the muscles, it would be interesting to compare cerebral atrophy with that produced by interruption of these afferent sensory impulses as produced by division of the posterior roots of a limb. This operation has been performed in an attempt to relieve spasticity. Does a resulting muscular atrophy closely resemble cerebral atrophy?

DR. A. SILVERSTEIN: As to the significance of the Horner syndrome, this gave considerable concern as it suggested an early peripheral involvement of the left seventh nerve, but careful investigation revealed that this was a congenital condition.

Whether or not atrophy can result from cutting the posterior roots of the spinal cord, I am in no position to answer. It is known, however, that patients with tabes dorsalis as a rule do not show this form of atrophy, although it may occur. Dr. Spiller again repeated the statement that he made at a previous meeting of this society to the effect that although he admits that the parietal lobe can produce atrophy, he has yet to be convinced that the motor cortex may not also produce this same condition. Time did not permit a discussion with arguments against this point, but I may reaffirm that patients with hemiplegia in whom atrophy develops sooner or later have had sensory symptoms, whereas patients with hemiplegia without sensory changes as a rule did not show atrophy. One of the most convincing proofs against the motor cortex and the pyramidal tract disturbance producing atrophy of the muscle is a case reported by Dr. Spiller in 1900, in which he described a patient, aged 50, who had a spastic paraplegia with no sensory disturbances and no muscle atrophy, although the condition had existed for more than a year. Dr. Spiller stated, "the absence of distinct muscle atrophy was one of the most interesting features of this case. This is especially noteworthy as much as some of the cell bodies of the anterior horns of the spinal cord were diseased." I believe that this statement not only answers the question whether the motor cortex is not the cause of atrophy of the muscles, but also invalidates the theories first presented by Charcot and more recently by Joseph Kiss that the anterior horn cells of the spinal cord are responsible for this phenomenon.

CLONIC OCULOGYRIC CRISES IN EPIDEMIC ENCEPHALITIS. DR. A. M. ORNSTEEN.

The occurrence of oculogyric crises in chronic epidemic encephalitis is now well recognized. Observers have repeatedly stressed the tonic nature of the spasm, with an occasional reference to a clonic form of upward spasm of the eyeballs. This does not refer to the nystagmoid movements observed in many cases of tonic spasm. The movements are rhythmic and rather slow, with a wide amplitude of excursion. Jelliffe (*J. Nerv. & Ment. Dis.* **69**:59 [Jan.]; 165 [Feb.]; 278 [March]; 415 [April]; 531 [May], and 666 [June]), has collected all reported cases of oculogyric crises and published a résumé of the accounts up to and including 1928. At least 100 authors have reported some 200 cases. In reading this résumé, I found only 12 papers referring to clonic spasm, showing that the tonic form is far more frequent than the other.

Up to the appearance of the case reported in this communication, we had not observed a case of clonic oculogyric spasm in the outpatient department of the University Hospital. Dr. Spiller called my attention to the rather unusual description of the attack given by the patient, although we were not able to confirm the statements until a later date. The patient described the attack as consisting of a "terrific pulling" sensation, back of the eyes, so that they seemed to bulge forward and diverge. This was followed by up and down movements of both globes, with widening of the palpebral fissures. The attacks were said to last for from one to twelve hours and were accompanied by the usual anxiety and agitation that most patients manifest during these attacks. The thought was expressed at first that the widening of the palpebral fissures and the subjective sense of bulging of the eyes might suggest an expression of the pathologic mechanism in the form of hypersympathicotonia, but dilatation of the pupils during the attack was not observed.

The characteristics of the spasm were later recorded by moving picture (which was presented). This showed a rhythmic oscillation of both eyeballs, symmetrical in timing and amplitude, which is approximately one movement a second or slightly less through an arc of about 45 degrees from the midposition upward. The upper

lids are retracted at each elevation of the eyes. The pupils are in the midposition of dilatation, but do not vary in width during the attack. By diverting the patient's attention to the performance of active movements elsewhere, the spasm is temporarily interrupted, but only recurs and continues for sometimes the best part of a day, requiring confinement in bed because of photophobia and general uneasiness.

The patient, C. I., a man, aged 25, was in the fourth year of a dental course when he had to discontinue all activities. He had acute encephalitis in 1923, beginning with amblyopia and diplopia, and followed by insomnia for three months, with diurnal somnolence. Hazy vision persisted; then the speech and walk became disturbed. At presentation, he spoke quickly, with a tendency to palilalia, and he salivated excessively. He had all the earmarks of a moderately advanced form of parkinsonism. The eye attacks were the last of the manifestations to develop up to the present time.

DISCUSSION

DR. J. C. YASKIN: I recognized this patient by the photograph, and have no doubt that this is a case of encephalitis. I was impressed with the emotional attitude. When he first came to me a few months ago, I gave him some distilled water hypodermically. The following week he stated that he had had only one spell. In the course of a few weeks he stated that he felt so much better that he thought that he would be able to procure some work. Then he disappeared. I do not mean to imply that this is a case of hysteria, but it is interesting to note how the patients in organic cases can be influenced by suggestion.

HEMATOMYELIA. DR. GEORGE WILSON and DR. REUBEN LEWIS.

This case was presented to the Society as a follow-up of the case presented at the meeting of December, 1930. The patient, J. H., a man, was brought into that meeting on a stretcher and was shown as a case of hematomyelia with quadriplegia. An injury had taken place on Oct. 4, 1930, when he fell down a flight of stairs. Following a gradual onset of symptoms, he was admitted to the Philadelphia General Hospital with an almost complete quadriplegia and a loss of sensation below the first rib anteriorly. This was on the tenth day following the injury.

A lumbar tap on the twelfth day showed yellow spinal fluid. On the thirteenth day there was distention of the lower part of the abdomen, and catheterization of the bladder yielded 34 ounces (895.38 cc.) of urine. On the next day, the patient was incontinent, but following this he regained control of the bladder. Jugular compression on the twenty-third day failed to show a rise in the pressure of the spinal fluid in the lumbar subarachnoid space. On the thirtieth day, a combined lumbar and cisternal pressure study was done. This showed a partial block between the needles.

On November 27, the fifty-fourth day after the accident, a lumbar tap showed no block, and when the patient was presented to the Society in December, he had regained a slight amount of power in the hands, and was able to flex the knees and extend them while lying on his back in bed.

Today the patient has regained much power and control of the extremities. He walks with a slightly spastic gait, but the Romberg sign is negative, and there is no clonus or Babinski sign. There is atrophy in some of the small muscles of the hands, and the triceps muscles are weak. There is some atrophy of the right triceps, and the tendon reflex is not elicited. Sensation has returned, and examination failed to show impairment to touch, pain, vibration, heat or cold, or stereognosis.

We present this as a case of hematomyelia at the level of the fifth, sixth and seventh cervical segments.

THE SURGICAL TREATMENT FOR CHRONIC SCIATIC PAIN. DR. WILLIAM J. TAYLOR.

I shall not attempt to detail the symptoms of chronic sciatica, but shall confine myself to a statement of my personal experience of the operative treatment for this condition. Most cases of chronic sciatic pain are due to lesions of the spinal, sacro-iliac or hip joints, and some are due to intra-abdominal inflammation or pressure, but a certain number are due to a lesion in or about the nerve itself, frequent perineuritis with adhesions, either alone or in combination with neuritis. All of my patients had been under treatment for long periods by rest in bed, counter-irritants, baking, electricity and salicylates.

In every case there had been exposure to extremes of heat, cold and dampness, and some patients gave a history of trauma. The cases may be classified into three groups or types: 1. Those in which the patients are free from pain while at rest, but have pain on exercise or on assuming special positions in bed. 2. Those in which there is a certain amount of pain when the patient is at rest, which becomes intense on exercise or assumption of a particular position. 3. Those in which the pain is of an indefinite character, present at rest, off and on, and sometimes improving to a certain extent with exercise.

In the first type, the inflammation of the nerve has subsided, but adhesions have developed. These may be fine or densely fibrous; the mode of action is clear; they drag on the nerve and produce pain. This is the type of case best suited for operation. The second type, in addition to adhesions about the nerve, has an actual inflammation of the nerve itself. Some of these patients may be cured by operation. The pathologic process of the third type is not clear; there can be no adhesions, and an operation can offer little chance of relief.

In practically all of my cases the nerve has shown some abnormality, usually a high bifurcation and anomalous branches which may extend into the sacro-iliac notch.

The objection has frequently been raised that as adhesions will form again at the seat of operation, why operate? My answer is that the adhesions in perineuritis are limited in area, thus permitting the nerve to be pulled on at some one or more points, whereas when the nerve is freely stripped of all adhesions, adhesions do form, but along its whole length, thus giving it a firm backing.

In one case, in which an old woman has not been materially benefited, it is possible that my diagnosis was wrong. Another old woman, with osteo-arthritis of the knee, after the operation had foot drop from which she is gradually recovering. Possibly some of the fibers of the nerve may have been injured at the time of operation. The other patients in my series have been relieved from pain and have been able to resume their occupations. These observations extend over a period of nineteen years.

In three cases my incision was not long enough to expose the nerve thoroughly; a second operation was done, other adhesions were found, and the nerve was released. The patients have been perfectly comfortable since the second operation.

Drainage of the wound is most important.

I have operated now twenty-four times, and my assistant, Dr. George W. Wagoner, has operated in eight cases. All patients have made satisfactory recoveries, with the exception of two, one already mentioned and another, also an old woman with osteo-arthritis of the hip and knee on whom I operated only in the hope of giving some relief from pain and on her urgent request.

The Operation.—My rule is to make a free incision, from the gluteal fold downward, of sufficient length to expose the nerve as far as the pain and tenderness extend on the thigh. The nerve is then hooked up with the finger, and the adhesions surrounding it are carefully dissected away. By this, I do not mean to stretch the nerve; I merely lift it up and take great care not to stretch it. All adhesions are then dissected off the nerve with a knife, or scissors if they are very firm, but they may be so fine that they can be stripped off with the fingers or gauze; all loose ends and tags of adhesions must be removed. Great care must

be exercised not to cut any of the branches of the nerve, which is then dropped back into its bed, the muscles are adjusted into their places, and the wound is sutured. The fascia should be sutured, and a drain of rubber dam inserted, to be removed in twenty-four hours.

In my first case there was a very high bifurcation of the nerve, with firm adhesions binding the two branches together and firm adhesions surrounding the nerve. This man has had no return of pain in nineteen years. In my second case there was an anomalous branch springing from the posterior surface of the nerve and passing to the muscles on either side, like an inverted Y, overriding the nerve. Underneath these branches there were dense adhesions. The man had suffered horrible pain on the least movement for eighteen months, and experienced complete relief from the moment he regained consciousness from the anesthetic, and had been free from pain up to four years ago when he was last heard from, a period of fourteen years.

The patient is kept in bed for three weeks; no splint is used, and the limb is placed on a pillow. He is then allowed to get up and walk about the ward and in four weeks to go home.

There has been no mortality, nor have there been any complications; all patients made rapid and uninterrupted surgical recoveries. I believe, therefore, that this method of treatment is worthy of more extended trial in properly selected cases of chronic sciatic pain, and that the operation is free from risk to life, and offers almost certain relief.

DISCUSSION

DR. W. G. SPILLER: At what period in the course of the progress of pain does Dr. Taylor call the condition chronic? How long does he wait before he recommends this operation? Has he performed it in bilateral sciatica?

DR. J. H. LLOYD: In 1916, I published a paper with Dr. A. C. Wood on the surgical treatment for sciatica, which came out in the Philadelphia Hospital reports. That paper was based on several observations of mine in my services at Blockley and at the Methodist Hospital. The idea of exposing the sciatic nerve and splitting the sheath first occurred to me about twenty years ago, when I saw an autopsy on a man who had died of intercurrent pneumonia during a severe attack of chronic sciatica. There was evidence of involvement of the trunk of the sciatic nerve with some adhesions. This suggested to me an operation by splitting the nerve sheath and draining. In ancient times the Chinese were said to have treated sciatica successfully by nerve puncture. They did not know much about the anatomy, but they used a long needle and thrust it in, thus probably securing drainage in some cases. The first operation that I had done was performed by Dr. Wood on a man who had suffered for a long time. Dr. Wood exposed the nerve, slit the sheath and irrigated the wound with physiologic solution of sodium chloride. The patient made a satisfactory recovery. It took some weeks for him to gain thorough relief from the pain, but the operation left him in a good condition. Not long after that, I had a case of severe sciatica at the Methodist Hospital. The patient was operated on by Dr. James Hutchinson. In that case also the nerve sheath was slit, and the man was relieved. I do not recall that I had ever heard of this operation before the idea was suggested to my mind at the autopsy that I have mentioned.

DR. N. W. WINKELMAN: I had known of Dr. Taylor's interest in sciatica for a long time, but I was unwilling to subject a patient to his operation until I had a patient suffering from this condition who seemed unable to obtain relief by any other means. I was forced to resort to this operation in this case; it had not responded to all known methods, and the patient demanded Dr. Taylor's procedure. Dr. Wagner, who is associated with Dr. Taylor, operated on this patient, and immediate relief was experienced.

DR. A. GORDON: In my experience there is no rule for the treatment for sciatica. I recall now a case in which a prominent physician told me that his

mother, 70 years old, had been suffering for a number of years from this condition. She had tried all kinds of remedies. I asked him to let me try a little remedy that in some cases gave relief. I injected hot saline solution — 20 cc. once and 30 cc. later — into the sciatic nerve. The woman is living now and has been well for some years. She had been a sufferer for many years, but in spite of the chronicity is apparently cured. In another case, hot distilled water gave relief. A sister of a prominent physician was also troubled with this condition. She was treated for sciatica for two or three years, but found that the pain was due to a tumor of the sacrum. There cannot be standardized rules and means. Each case must be studied individually.

DR. F. H. LEAVITT: At the Orthopedic Hospital all cases of chronic sciatic neuritis are thoroughly studied, and in the cases in which the condition has been present for many months Dr. Taylor is consulted. In no case in which he has operated has there been a failure of complete recovery. He generally keeps the patient in bed for four weeks. Sciatic neuritis amenable to this type of treatment is found most frequently in the laboring man who is exposed to extremes of heat and cold and dampness, plus constant pressure on the buttocks, as from sitting on the hard seat of a motor truck or the gunwale of a boat.

DR. W. J. TAYLOR: In answering Dr. Spiller's questions I would say that I have never operated on a patient under several months unless the pain was unbearable and the patient disabled, and even then with the fear that it might be too early. Most of the patients have been disabled for a year or more. Many have been chauffeurs, those exposed to extremes of heat and cold. I have never operated in a bilateral case, as that would suggest a central cord lesion. These adhesions are often very dense, and as soon as they are relieved, the pain is gone. The difficulty is to select the case and to operate carefully, never stretching the nerve, and handling it with extreme care.

I have very little more to say other than that there are only a limited number of cases in which operation should be performed. The best results are secured after the acute neuritis has subsided in cases in which adhesions have formed, binding the nerve down. I have never seen any ill effects. Recovery is prompt and permanent.

PALM AND SOLE PATTERNS IN IDENTICAL TWINS. DR. FREDERIC H. LEAVITT.

Dr. Leavitt presented studies of palm and sole patterns in identical twins, and demonstrated their marked similarity.

DISCUSSION

DR. J. H. LLOYD: It is accepted by many that the close resemblance of identical twins to each other is evidence that they are developed from the same ovum. The subject is not new. The first case that I know of on record was referred to by Dr. Benjamin Rush in his book on diseases of the mind, published in 1812. This was the case of twin brothers who looked so much alike that no one could tell them apart. They both served in the Revolutionary War as commissioned officers. After the war they settled in New England and lived separate lives. The same mental disease developed in both at about the same age, and both committed suicide. Francis Galton refers to several interesting cases of twins who were undoubtedly of the identical sort. It is necessary to take into account the possibility of imitation in children; when twins live together, if a fit develops in one child, the other may imitate it. I suggest this only as a possibility.

DR. I. MYERS: Since identical twins result from the symmetrical splitting of a single ovum, although they represent cells containing the same kind of chromosomes there is nothing, *a priori*, to lead one to suspect that the finger-prints and sole-prints would be identical or almost so — right corresponding to right and left to left. The right of one twin and the left of another might, for instance, have

been identical, and the other right and left have been respectively different from each other. It is noteworthy that there is usually, however, no transposition of viscera in one of identical twins. It seems as if certain forces associated with the polarity of the ovum govern the position of finger prints in unioval twins as well as the side on which the various viscera occur.

DR. F. H. LEAVITT: Much literature has appeared recently on identical twins. This case is presented particularly in relation to the studies on the palm and sole. I believe that it would be interesting to investigate children with one parent who has had mental disease, to see whether the child's palm and sole patterns partake more of the diseased parent's palm and sole patterns than of those of the normal parent. In this way one may be able to develop prognostic criteria that may prove of value.

NEURITIS AND MULTIPLE NEURITIS FOLLOWING SERUM THERAPY. DR. SAMUEL B. HADDEN and DR. GEORGE WILSON.

(From the Neurological Department of the School of Medicine, University of Pennsylvania. The cases on which this paper is based were studied at the Abington Memorial Hospital, the Philadelphia General Hospital and the University Hospital.)

With the increased use of therapeutic serum in the past twenty years, much has been written of the various manifestations of anaphylaxis. Urticaria, arthralgia, adenopathy and cardiac collapse are well known complications of serum therapy. Coma, and occasionally death, have been reported following the injection of serum. Many reports of multiple neuritis and myelitis following the use of the Pasteur treatment have appeared, and encephalitis following vaccination is well known. Another unpleasant complication of prophylactic efforts, fortunately one less frequently seen, is multiple neuritis.

In 1912, Thaon (Neuritis Following Prophylactic Injection of Tetanus Antitoxin, *Rev. de méd., Paris* **32**:749 [Sept.] 1912) reported a case in which paralysis of the serratus magnus and other muscles developed following serum sickness due to the injection of 10 cc. of tetanus antitoxin. In 1915, Richardson (Tetanus with Recovery and Secondary Multiple Neuritis, *J. A. M. A.* **68**:1611 [June 2] 1917) reported a case of severe tetanus with recovery, which was followed by pronounced multiple neuritis which he attributed to the action of the tetanus toxin. Dyke (Peripheral Neuritis After Tetanus Antitoxin, *Lancet* **1**:570, 1918), in 1918, wrote on neuritis following the prophylactic injection of tetanus antitoxin, and considered it to be allergic. André-Thomas (Neuritis Following Serotherapy, *Presse méd.* **33**:217 [Feb. 18] 1925) cited two similar cases, one following the administration of antidiphtheric serum and the other after antistreptococcic serum.

Souques, Lafourcade and Terris (Polyneuritis Following a Prophylactic Injection of Antitetanic Serum, *Bull. et mém. Soc. méd. d. hôp. de Paris* **48**:757 [May 23] 1924), Lechelle, Thévenard and Lacan (A Case of Neuritis Following an Injection of Antitetanic Serum, *Bull. et mém. Soc. méd. d. hôp. de Paris* **50**:1277 [July 16] 1926), Katz (Anaphylactic Polyneuritis After Inoculation for Tetanus, *Deutsche med. Wchnschr.* **53**:1637 [Sept. 23] 1927), Folly (Partial Neuritis of the Brachial Plexus After Injection of Antitetanic Serum, *Strasbourg-méd.* **86**:90, 1928), Crouzon and Delafontaine (Case of Serum Neuritis, *Bull. et mém. Soc. méd. d. hôp. de Paris* **50**:1049 [June 18] 1926), and Baudouin and Hervi (*Rev. neurol.* **1**:306 [March] 1931) have reported cases of neuritis following the use of tetanus antitoxin. We have had the opportunity of observing six cases.

CASE 1.—A white boy, aged 17, was seen first on June 8, 1929; he had received a puncture wound in the thumb in May, 1929, for which he was given 1,500 units of tetanus antitoxin in the left side of the chest posteriorly, just below the scapula. A few days later, hives developed over the entire body. The hives lasted for two or three days, and the day following their disappearance he awoke with severe pain in both shoulders. Heat relieved the pain in the right shoulder, but it persisted in the left. On the eleventh day after the serum injection, paralysis developed in the movements of the left shoulder. This condition persisted up to

the time he was first seen. Examination showed a left circumflex palsy, with anesthesia in the nerve area and only slight response of the nerve to faradism. The supraspinatus and infraspinatus muscles were similarly affected. Later, a complete reaction of degeneration was found in the affected muscles, which became profoundly atrophic. After four months, improvement began. An occurrence of interest in this case was numbness of the right side of the face and of the whole right side of the body which developed on July 8, approximately two months after the injection. There was no disturbance of reflexes at this time. Pain, touch and vibration sensibility were all diminished on the right side. This condition was not associated with any generalized symptoms and cleared up within a few days; it may have been the result of a cortical edema. Reexamination of the patient on May 8, 1931, disclosed that he had entirely recovered.

Case 2.—A white boy, aged 7, in May, 1931, had a laceration of the right ear and was given 1,500 units of tetanus antitoxin in the left deltoid. A localized urticaria developed on the following day at the point of injection, and quickly disappeared. On May 19, seven days after the injection, he was admitted to the Abington Memorial Hospital with serum sickness. He had swelling and redness at the point of injection and a generalized arthralgia. On the day following admission, or thirteen days after the serum was given, left musculospiral palsy developed, which was associated with adenopathy in the left axilla. The reflexes and sensation in the affected extremity were normal. The muscles responded very feebly to a strong faradic current. At the end of six weeks of treatment, which consisted of protecting the paralyzed muscles against deformity and the administration of massage and faradism, the patient made a complete recovery.

Case 3.—A white man, aged 40, a fireman in the Department of Public Safety, whose case was reported by Dr. Owen and Dr. Hadden and is found in the Proceedings of the Academy of Surgery of Philadelphia, May 4, 1931, gave the following history: On Dec. 18, 1930, he suffered a puncture wound of the right foot for which, as a prophylactic, he was given on the following day 1,500 units of tetanus antitoxin into the anterior abdominal wall. On December 25, a severe generalized urticaria developed, which was relieved by the injection of epinephrine. On December 28, he was awakened during the night by a very severe pain in the neck, which was worse on the right side; he also had pain in both shoulders, hands and forearms and in the interscapular area. He could not move the fingers and wrists, and he said that they felt swollen and tingled greatly. The pains and paresthesias continued until the end of the first week in January. Power in the left upper extremity recovered quickly, and by January 5 was normal except for slight weakness in the hand grasp. At this time marked weakness in the grip of the right hand and about 70 per cent loss of power in the extensors of the wrist were noted. He complained of paralyzing pain in the neck, shoulders, interscapular area and both arms. Pressure over the muscles of the right side of the neck, in the right axilla and over the nerve trunks caused severe pain. On abduction of the arm at the shoulder, which caused stretching of the nerve trunks in the axilla (a Lasègue sign in the upper extremity) severe pain was elicited. No objective impairment of sensation was detected. The tenderness of the nerve trunks was present in the left arm, but to a much less degree. The right biceps and triceps muscles were weak, and their reflexes were not obtained, whereas those on the left were normal. The paralysis improved rapidly, and by January 19, one month after the injury, the patient was able to return to active duty. A recent examination revealed that power in both arms and hands was normal. There was a moderate winging of both scapulas. The patient stated that subjectively his arms and hands did not feel as strong as before the neuritis developed.

Case 4.—A white boy, aged 17, on admission to the University Hospital, on Nov. 10, 1930, stated that he had been shot in the right popliteal space; he was immediately given tetanus antitoxin intramuscularly in the left thigh. On November 16, there developed a swelling of the right thigh and knee with severe local pain. On November 17, he experienced pain in the arms from the elbows

upward into the neck, so severe that he could not sleep for four or five nights. During the next ten days he could not move the head from side to side without great discomfort. The pain disappeared by December 1, and after that he had only occasional shooting pains in the right arm. Weakness was associated with the pain and became more apparent as the pain disappeared. The left arm had improved so that the patient was able to perform all movements with comparative ease, but there was definite weakness. At present he cannot elevate the right arm at the shoulder at all, nor can he abduct it or raise it behind him. He can flex and extend the arm at the elbow, but the power is not good. Other movements of the right upper extremity cannot be performed well. Electrical examination of the muscles involved showed reactions of degeneration in the right deltoid, supraspinatus and infraspinatus muscles, and in the left deltoid. The only sensory disturbance noted was loss of pain, heat and cold sensation in the right circumflex area.

CASE 5.—A white man, aged 31, had a mild attack of diphtheria in the latter part of October, 1930; he was treated with antitoxin. A severe neuritis developed about November 1; he had been released from quarantine and was entirely well for two days before the neuritis began. During the eight days of quarantine he had what he termed a "dropped palate," but he had neither nasal speech nor regurgitation of fluids through the nose. The pain that developed ran from the right shoulder to the right side of the neck and down to the elbow. The same distribution of pain was present on the left, but was only half as severe. The neuritis persisted for three weeks. The right deltoid was greatly atrophied, the left slightly. The biceps muscles functioned well; the left triceps was a little weak, the right normal. There was analgesia in the circumflex area on the right, the area for the loss of pain being smaller than that for touch and temperature, but touch was not entirely lost in any part. On the left, the impairment of sensation was slight in the corresponding area. He had complete deltoid paralysis on the right; he could elevate the left upper extremity above the shoulder, but when resisted the power of movement was poor. Both upper extremities tired quickly. The lower limbs were not affected, although the knee jerks were weak. The achilles reflexes were normal.

CASE 6.—A white girl, aged 17, was admitted to the University Hospital on May 5, 1931, for study of a progressive paraplegia of five years' duration. An added factor in the history, however, was that she had never had trouble with the arms until she had an acute illness in March, 1931, and was given an intramuscular injection of diphtheria antitoxin in the right buttock. Three days after the injection, severe pain suddenly developed in the shoulders. On the next day, both hands became swollen, particularly the fingers; the palmar aspect of the right hand was painful, but not the left. The pain in the right shoulder region was excruciating, and she could not elevate or move the right arm because of the pain, which lasted for about two weeks. Following the disappearance of pain, she experienced generalized weakness in the right arm. At present she has a moderate degree of atrophy of the right supraspinatus and infraspinatus muscles, as compared to the left. Rotation of the right humerus is accomplished with much less power than on the left. She states that the entire right hand and arm are weak. Sensation is normal.

Comment.—Most cases of neuritis following serum therapy reported in the literature have followed the injection of tetanus antitoxin; some developed after the injection of diphtheric antiserum, and one followed the injection of antistreptococcic serum. It is granted that multiple neuritis is a common complication of diphtheria. Jackovleva (Diphtheritic Polyneuritis After [Inadvertent] Injection of Diphtheria Toxin, *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **47**:203, 1927) reported multiple neuritis following the inadvertent injection of diphtheric toxin mistaken for a toxin-antitoxin mixture, several cases proving fatal. It is our belief, however, that with the early injection of diphtheria antitoxin and the resulting neutralization of the toxin, these complications are avoided, and today, when they do occur, many

are the result of the anaphylactic serum reaction. This is borne out by several cases in the literature and those here reported, when, after apparent recovery from mild diphtheria and during the serum sickness, multiple neuritis developed. In tetanus, multiple neuritis does occasionally occur, but it is rare. Hnatek (Tetanus and Neuritis, *Wien. med. Wchnschr.* **55**:997, 1905) reported a case in which it occurred although antiserum was not employed, but in cases in which tetanus never develops and only the antitoxic serum is given, it is unconceivable that there should be enough unneutralized toxin in the serum to cause neuritis without causing clinical symptoms of tetanus.

No case of this condition has come to autopsy, so that the neuropathologic condition has not been definitely determined. Mason (Optic Neuritis in Serum Sickness, *J. A. M. A.* **78**:88 [Jan. 14] 1922) reported four cases of optic neuritis and described one in detail. Optic neuritis developed in three of his patients following the injection of antipneumococcic serum, and in one following the use of antimeningococcic serum. The optic neuritis in all cases developed during serum sickness and subsided with complete recovery when the serum sickness disappeared. Kennedy (Symptoms Induced by Angioneurotic Cerebral Edema, ARCH. NEUROL. & PSYCHIAT. **15**:28 [Jan.] 1926) reported severe symptoms referable to the central nervous system in patients subject to angioneurotic edema, in which presumable focal edema of the brain existed. We have observed a case of allergic migraine and hay fever with jacksonian epileptiform attacks, in which the removal of wheat from the diet gave relief from the symptoms for two years. It is our belief that edema develops in the nerve trunks, similar to the urticarial swelling in the skin. Both of these structures are of ectodermic origin, and this may explain their common reaction. The selectivity for the nerves of the brachial plexus is difficult to explain. Baudouin and Hervi explained this selectivity by chronaxia, pointing out that various toxins, such as lead, manifest a selectivity toward nerves possessing certain chronaxies, and that the reaction from serum injection picks out the nerves with low chronaxia.

In reporting these cases and emphasizing their serious complications we are fearful that consideration of the facts might deter physicians from the use of antiserums in proper cases. That is far from our purpose; we do suggest, however, that more careful testing for horse serum sensitization should be employed, and that desensitization be resorted to when indicated. Today, when the free administration of diphtheria toxin-antitoxin mixture is employed, it is well to bear in mind that this is sufficient to render a patient sensitive to horse serum. We also call attention to the remark of Braunlick (Anaphylaxis Following the Injection of One Thousand Five Hundred Units of Tetanus Antitoxin, *J. Iowa M. Soc.* **17**:450 [Dec.] 1927), who reported that serum sickness occurs much more frequently and is more severe following the use of fresh serum than when older serum is employed.

Conclusions.—1. Neuritis and multiple neuritis are occasional complications of serum therapy, and we regard them as anaphylactic phenomena. 2. The brachial plexus, especially the upper cord, is most frequently involved. 3. More careful tests for sensitization and desensitization should be employed before antiserums are given.

DISCUSSION

DR. W. G. SPILLER: The clinical picture in many of these cases of neuritis following antitoxin injection is of a definite type, regardless of the part of the body in which the injection has been made. In my three cases recorded in the paper just read (cases 4, 5 and 6), the injections were given in the thigh, the upper arm and the buttock, respectively, but all three patients presented almost an identical clinical picture. Usually about the eighth or ninth day after the injection, when this complication results, severe bilateral pain is felt in the neck and shoulder, extending into the upper limb on each side, i. e., in the distribution of the uppermost roots of the brachial plexus. This is followed by atrophy and paralysis, especially of the deltoid muscle. The left side seems to recover first, although

in the first two cases of Wilson and Hadden's paper this side was the more affected. It may be interesting to note that in these two cases, the injections were made into the left deltoid muscle and near the posterior border of the left scapula, respectively. The paralysis is likely to persist for some time. My first patient, the boy who had been shot, had a complete right deltoid paralysis when he came to me, but by throwing the entire limb upward with a swinging movement he gradually improved and became able to elevate the limb slowly.

The serum paralysis has recently been discussed in the Neurological Society of Paris, and the proposal has been made that a commission should be appointed by the Academy of Medicine to study the question. Damages have been awarded to the plaintiff in France when preventive antitoxin injection had not been employed.

DR. A. GORDON: Tonight's story deals with therapeutic accidents from the use of antitoxin. In a recent contribution (*M. J. & Rec.* **127**:550 [May 16] 1928) I reviewed two cases of serum disease from serum used for immunization. The two cases were almost identical. One was in a boy aged 11, and the other in a boy aged 19. The physician advised a prophylactic injection for immunization from scarlet fever. The first patient was given 250 units, and paralysis of the musculospiral nerve developed. The same condition also developed in the other. The paralysis developed on the side opposite the seat of the inoculation, so that there could be no question of a mechanical damage to the nerves or of ascending neuritis. The probabilities are that there is a damaging effect of the serum on the roots of the peripheral nerves. Fortunately, the children completely recovered in three or four weeks, but there was talk of prosecution. In order to avoid these possibilities, I believe it is advisable (from a medicolegal standpoint) to get permission from the parents before performing the inoculation. In addition to Dr. Wilson and Dr. Hadden's cases of therapeutic serum disease, there are also cases of prophylactic serum disease to be considered, but all such cases bear a favorable prognosis.

A CASE OF PRIMARY TUMOR OF THE GASSERIAN GANGLION. DR. MELBOURNE J. COOPER.

The symptom-complex of involvement of the gasserian ganglion by a tumor or a tumor-like process, with little or no implication of the other structures of the central nervous system, is seen infrequently enough for such a case to merit report. Hellsten (quoted by Cushing: The Major Trigeminal Neuralgias and Their Surgical Treatment Based on Experiences with Three Hundred and Thirty-Two Gasserian Operations, *Am. J. M. Sc.* **160**:157 [Aug.] 1920), in 1914, had collected 23 cases of tumor of the gasserian ganglion in the literature; Frazier (An Operable Tumor Involving the Gasserian Ganglion, *Am. J. M. Sc.* **156**:483 [Oct.] 1918) had found 13 cases in which operation had been performed, including his own 3 cases, reported in 1918; and Cushing, in 1920, mentioned the occurrence of 8 tumors of the gasserian ganglion in his series of 550 intracranial tumors verified by operation or autopsy. Of the 8, 4 were endotheliomas and 4 were tumors arising in structures outside the dura.

The patient whose history is here reported was seen at the Hospital of the University of Pennsylvania on the respective services of Dr. William G. Spiller and Dr. Charles H. Frazier. The outstanding features were early spontaneous pain in the distribution of the auriculotemporal nerve, with objective sensory disturbances in the inferior maxillary distribution, progressing to a combination of spontaneous pain, hypesthesia and hypalgesia throughout most of the left trigeminal distribution, and left-sided deafness. The clinical manifestations of tumor of the gasserian ganglion are usually stated to be such progressive disturbances of subjective and objective sensations in the distribution of the trigeminal nerve on the side of the lesion. Paralysis of the motor division frequently occurs, and Spiller (Tumor of the Gasserian Ganglion, *Am. J. M. Sc.* **136**:712, 1908) has found degeneration of the motor and sensory nuclei in one of his reported

cases. The involvement of other cranial nerves by tumors arising from the region of the gasserian ganglion has been mentioned by Dercum, Keen and Spiller (Endothelioma of the Gasserian Ganglion, *J. A. M. A.* **34**:1026 [April 28] 1900), Plumer and New (Tumor of the Middle Cranial Fossa Involving the Gasserian Ganglion, *J. A. M. A.* **62**:1082 [April 4] 1914), Cadwalader (On the Symptomatology and Diagnosis of Intracranial Tumors, *J. Nerv. & Ment. Dis.* **44**:11 [July] 1916), Frazier, Spiller and others. The first, second, third, fourth, sixth, seventh and eighth nerves seem to be most subject to invasion or direct pressure in the experiences of these observers. Cadwalader has called attention to the importance of considering the order of appearance of the symptoms of multiple cranial nerve involvement as being essential for localization, and (Significance of Facial Pain in Determining the Location of Intracranial Tumor, ARCH. NEUROL. & PSYCHIAT. **4**:182 [Aug.] 1920) in another communication he stressed the significance of facial pain and anesthesia, followed by deafness, as indicative of the presence of a tumor involving the gasserian ganglion. Spiller considers enlargement of the lymphatic nodes of the neck as having diagnostic value.

Attention has been directed to the differential diagnosis between tumor and syphilitic or tuberculous meningitis by Spiller and Frazier, and Dr. F. C. Grant reported before the Philadelphia Neurological Society on May 25, 1924, the case of a patient with syphilis, who was found at an operation to have an endothelioma of the gasserian ganglion.

Clinical History.—I. H., a man, aged 65, was admitted to the Hospital of the University of Pennsylvania on the service of Dr. Spiller on June 6, 1930, complaining of pain in the left temporal region for seventeen months. Six months prior to admission he had noticed an enlargement of the upper cervical lymphatic nodes on the left side; two months later, numbness of the left half of the chin and upper lip had developed; shortly before admission, he had felt a tickling sensation and a sense of fulness in the left ear. He had lost about 36 pounds (16.3 Kg.). He had had a mild diabetes and repeated attacks of what he called "la grippe."

Examination.—The man was cachectic and had a firm, fixed mass, the size of a hen's egg, in the region of the left upper cervical lymphatic nodes. He had spontaneous pain of a dull, constant type in the area of distribution of the left auriculotemporal nerve, and hypesthesia and hypalgesia in the lower anterior portion of the cutaneous distribution of the left inferior maxillary nerve and in a small part of the upper lip. There was some disturbance of sensation in the gums of the left side and on the left side of the tongue, but the sense of taste was preserved. The tongue deviated toward the left on protrusion. There was congenital cataract and microphthalmia of the left eye, so that the pupillary reactions on that side could not be evaluated, but there were no other indications of ocular muscle palsies. The Wassermann test of the blood was negative.

It was feared that the enlarged lymphatic node might be malignant, but clinical and roentgenologic studies failed to show definite evidence of a primary focus. The patient was referred to Dr. Frazier for a biopsy of the tumor of the neck. The microscopic report on the tissue removed at that time was not conclusive at first. Dr. Bothe's final conclusion, some months later, was that it was metastatic carcinoma.

Course.—The patient left the hospital shortly after the biopsy, and the diagnosis at that time was metastatic carcinoma of the lymph glands of the neck, but the primary focus was still uncertain. Dr. Spiller made the following note on June 21, 1930: "It is uncertain whether the left side of the tongue is atrophied or not. It seemed so when the patient first came into the ward, but at present atrophy and fibrillary tremors are not distinct. . . . The man may have a tumor of the gasserian ganglion, but the pain is not so severe as it usually is in ganglion tumor, and it is confined to the auriculotemporal branch. This very limited distribution of pain is peculiar for a ganglion tumor. The anesthesia

also is of very limited distribution. I have been inclined to regard the sensory findings as caused by involvement of the third division from the tumor of the neck."

Readmission.—The patient was readmitted to the service of Dr. Spiller on March 15, 1931. At that time there was spontaneous pain throughout the entire left trigeminal nerve distribution, and also almost complete anesthesia and analgesia in most of the same area. An indurated, firm mass beneath a thin layer of soft tissue had developed in the left lateral pharyngeal wall; the left vocal cord had become paralyzed, and hearing in the left ear had become much impaired or possibly lost. Dr. Frazier believed that the combination of spontaneous pain and hypesthesia, progressing to involve the entire left trigeminal nerve distribution, could be explained only by the presence of a tumor of the gasserian ganglion. He operated on the patient on April 1, and when the ganglion was exposed it was found to be adherent to the dura and was three or four times its normal dimensions. The floor and base of the skull beneath the ganglion had been eroded. Dr. Frazier's operative diagnosis was tumor of the gasserian ganglion.

At the time of operation, frozen sections of the ganglion tissue were made, and Dr. Bothe examined them microscopically. He considered that the tissue was that of an endothelioma. Dr. B. J. Alpers later examined sections that had been prepared by other methods of fixation, and was unable to confirm the provisional diagnosis of endothelioma. He found, instead, evidence of a chronic inflammatory process as the predominant picture, with nests of large cells having the appearance of epithelial cells scattered among the more abundant inflammatory elements. He believed that these cells were suggestive of carcinoma, but were not definitely carcinomatous, and because of the questionable features he submitted sections to Drs. Fox and Bothe for examination.

The patient was sent to the Radiological Department of the Philadelphia General Hospital, and died there on April 28. At autopsy, the brain showed no striking features, but the dura at the site of the operation on the gasserian ganglion was thickened, and the bone underlying the dura at that point was somewhat porous and crumbly. A piece of dura excised at autopsy was rubbery-hard in consistency and varied from 5 mm. to 1 cm. in thickness. Shallow ulcers filled with partly organized blood clot were present. The tissue did not resemble carcinoma grossly; some nodules were dissected out of the tissues of the neck, and there were some nodules suggestive of carcinoma in the lungs. No evidences of malignancy were found in the other organs.

Dr. Alpers exchanged sections with Dr. Winkelman for a comparison of the tissues obtained at autopsy with those obtained at operation, and after a study of the autopsy material he concluded that the dura from the site of the operation showed chronic inflammatory changes and the invasion of cells that were probably carcinomatous, but not certainly so; also, that the lymphatic nodes of the neck contained undoubted carcinomatous metastases.

Addendum.—Subsequently, Dr. Alpers prepared additional sections of the ganglion; his final report was: "The tissue is composed of a dense fibrous carpet in which lie numerous fibroblastic cells. Infiltrating this dense fibrous substance are numerous inflammatory cells. These are gathered into foci or scattered diffusely through the tissue. They are present in large numbers. The cells are chiefly lymphocytes and plasma cells, among which are scattered polymorphonuclear elements. Giant cells are nowhere in evidence. Scattered here and there are foci of cells with a large, oval, vesicular nucleus and a rather abundant cytoplasm. They look like epithelial cells, but cannot be definitely identified as such. No mitoses are seen among them. The bood vessels are thickened and in some places hyalinized. Here and there one sees the remains of ganglion cells. I find no positive evidence of carcinoma, though the tissue is very suspiciously suggestive. There is no question that a rather active chronic inflammation is present."

DISCUSSION

DR. W. G. SPILLER: My experience with tumors of the gasserian ganglion extends over many years, beginning with the case reported by Dercum, Keen and

Spiller in 1900. In 1908, I reported two cases, and these with a new case were later included in a paper by Frazier in 1918. In 1924, I referred another case to the Neurosurgical Department of the University of Pennsylvania, and the patient was presented by Dr. Grant before this society, but no published report was made. The symptoms in this case were typical of a tumor of the gasserian ganglion: The man had loss of the left corneal reflex, a sign described by Oppenheim as occurring with tumor of the posterior cranial fossa, atrophy of the muscles supplied by the left motor fifth nerve, hyperesthesia in the left fifth nerve distribution and numbness in the left side of the face. Anesthesia dolorosa in the fifth nerve distribution is an important sign of the ganglion tumor.

Horrax and Buckley have recently stated that an intrapontile tumor may clinically simulate an angle tumor. I will state from my experience that a tumor in this location may also simulate clinically a tumor of the sensory root of the gasserian ganglion, although a tumor in the pons is likely to become bilateral. A glioma in the pyramidal tract may allow many nerve fibers to pass through it, and cause less paralysis than one might expect.

Book Reviews

NEUROPSYCHE UND HIRNRINDE. By DR. N. E. ISCHLONDSKY. Band I: Der bedingte Reflex und seine Bedeutung in der Biologie, Medizin, Psychologie und Pädogogik. Ein Handbuch der experimentellen Reflexologie für Fachleute und Studierende. Paper. Price, 20 marks. Pp. 328, with 39 illustrations. Band II: Physiologische Grundlagen der Tiefenpsychologie unter besonderer Berücksichtigung der Psychoanalyse. Ein Handbuch für Studierende, Aerzte Psychologen und Pädagogen. Paper. Price, 22 marks. Pp. 356, with 15 illustrations. Berlin: Urban & Schwarzenberg, 1930.

These two volumes are written in German by a Russian living in Paris, who has had first hand experience with the methods of the Pavlov school applied to psychiatry. They are written in a clear, easily understandable style. Volume I gives a logical description and summary of the important work from the Pavlov school, beginning with a short description of the technic and including the details of some of Pavlov's recent investigations. The author quotes Pavlov in many places by whole paragraphs, although not in inverted commas, as for example, in the preface. The experiments are described in detail, in a more systematic and logical order than Pavlov follows in either of his two books. The book is enriched by many examples from actual human life, some of which come from Pavlov, but many are the author's own observations. The books make interesting reading, but contain rather more speculation than Pavlov would sanction.

The author takes sentences of Pavlov and expands them into several pages; for example, in dealing with the reflex of life from Pavlov's chapter on the reflex of purpose (chapter 28, lecture on Conditioned Reflex, International Publisher) in chapter 16, Ischlondsky devotes several pages to this. He introduces diagrams and makes schemas where Pavlov would not venture to be so positive.

Most of the laws of conditioned reflexes are illustrated by concrete experiments from Pavlov's laboratory. He adheres to Pavlov but goes further; for example, at the bottom of page 9, he says: "There is no indifferent agent that cannot be made by the method of conditioned reflex into a powerful stimulator of some activity of the organism, and vice versa there is no activity of the organism which cannot be connected with any of our chosen stimuli."

The conditioned response can be measured by: (1) the secretory, (2) the local motor, (3) the general motor, (4) the vasomotor, (5) the respiratory and (6) the electrogalvanic skin reactions.

Chapter I deals with the biology and philosophy of the conditioned reflex and the central nervous system as an equilibrating mechanism. The author considers that there are four chief fundamental unconditioned reflexes or instincts (p. 282) on which most of the others are built: the self-preservative reflex, the reflex of nutrition, the sexual reflex and the orienting reflex. The latter is considered as the basis for all investigations. Concerning the sexual reflex, he says (p. 288): "The whole development of the sexual reflex by the animal kingdom is in complete agreement with its general biologic rôle and all the analytic activity of the organism has been formed by virtue of the inner dependence of the sexual reflex. Recognizing this, countless phenomena which seem at first paradoxical can be understood. The mother instinct is in close dependence on the sexual reflex, and this in turn is the basis of the several instincts in which the love is not limited to the own child."

The connection between the conditioned and the unconditioned reflex is summarized thus: The conditioned reflex is a temporary connection in the answer of the organism to an external stimulus; it is not accidental, but occurs under definite conditions; the course of the conditioned reflexes is equally as law-obeying as that of the unconditioned reflexes but their origin and development are more complicated and labile than the unconditioned (p. 16).

The book begins with a discussion of the fundamental laws of the formation of conditioned reflexes—extinction, irradiation, inhibition, disinhibition, induction, etc. Copious examples are given: Extinction is illustrated by the reaction of the soldier on the battlefield to explosions of cannon; the first lively reactions (conditioned reflexes) disappear as they are not supported by the unconditioned stimulus (wounding). If the soldier, however, is away from the battlefield for some time, when he returns the first lively reactions may reappear, just as in the dog the extinguished conditioned food reactions reappear after a rest. The conditioned reflexes on the battlefield may be brought out also by supporting them by the unconditioned, e.g., after wounding (p. 85).

An example of irradiation causing epilepsy is taken from a patient in whom itching of the nose spread to the region of the arm due to their close association during the time that a skin graft was made from the arm to the nose (p. 71).

Many actual protocols are given and clearly explained.

The conception of induction as used by Sherrington and by Pavlov is discussed and, furthermore, applications from life are made, as when a dog pulls on a rope harder when it is jerked owing to the setting up of positive induction (p. 175).

Six fundamental mechanisms of the higher nervous activity are: excitation, inhibition, the movement of excitation and inhibition in the cortex, or irradiation and concentration; the phenomena of Schaltung; positive and negative induction, analysis; and to this is added the principle of the dominant discovered by Uchtomsky (p. 214). This is stated as follows: If there exists in the central nervous system an especially strong focus of excitation, then all excitatory impulses caused by the stimulation of different afferent paths are diverted from their usual course to this focus of excitation, so that these extra afferent impulses all call out not their own activity, but that of the greatly excited center. The conception of differentiation is made clear by diagrams (e.g., pp. 221 and 265), which Pavlov always avoids.

In the second volume, the author attempts to give the practical evaluation of the laws obtained by exact laboratory experiments described in the first volume and an objective analysis of human psychobiology. This task appears at first very vague, for nothing is known of the objective developmental mechanism.

The author attempts to explain all human activity on the basis of conditioned reflexes—culture, health, mental disease, etc. The importance of time as a factor in conditioned reflexes is illustrated by the necessity to observe periodicity in order to sleep efficiently, digest food, etc. Pessimism and optimism are explained as a predominance of inhibition or excitation (p. 10). On page 14 he says, "the entire life cycle of the organism represents a rhythmical progress, and if this rhythm is not cared for always and as shown by the method of conditioned reflexes, it can suffer deviations in adaptation to the reactions of the external milieu; on the other hand, the once elaborated rhythm cannot suffer too sudden a change, for this would result in a general serious disturbance."

Induction is the basis of the contradictory actions and the ambivalence of Freud and Bleuler; if the originally excited (or inhibited) point is weak, then the negatively (or positively) inducted point may prevail, giving the opposite effects (p. 21).

The formation of new conditioned reflexes of higher orders is much more common in the human being than it is in animals. The formation may occur by irradiation or by induction (p. 28).

An example is given of the production of a conditioned orgasm elaborated by the irradiation of excitation during the school life of a child with a weak nervous system (p. 31). The pupil feared scolding by the teacher for tardiness while trying to prepare his lesson: the feeling of hurry and impatience reaches a high tensity, and immediately there ensues a feeling of sexuality and orgasm. The original excitation spreads from the stimulated center by the law of irradiation, and, thanks to the labile constitution of the child, it reaches the sexual center and serves as a stimulus for the sexual reflex. Later on, any of the accompaniments of the original situation or their conditioned stimuli may call out this pathologic sexual reflex.

Masochism occurs when some painful stimulus or situation during early life coincides with a strong sexual excitation (p. 34). This is analogous in the dog to the conversion of a painful electric stimulus into a conditioned food signal.

He concludes that coitus had best occur at night because the following sexual inhibition passes quickly into sleep and no possible connection can be elaborated between the stimulus of the external world and the sexual inhibition following the sexual act (by induction), such as might lead to impotence; or secondly, inhibition in another center may be so strong as to pass over to the sexual center and this becomes inhibited; external stimuli falling on the organism at this time become conditioned stimuli for the inhibition of the sexual centers (p. 43). Thirdly, some strong stimulus occurring during sexual excitation, as a knock on the door, may by induction produce inhibition of the sexual center, and this, or some accompanying element of this situation, becomes a conditioned inhibitor of the sexual center. Fourthly, a parabiotic state may be caused by a collision of excitation and inhibition, so that strong stimuli have less effects than weak ones, for example, reading a letter may have more effect than the actual presence of the writer (p. 44).

Cases of Freud's psychoanalysis are explained as excitation or inhibition of conditioned reflexes (p. 50). Regarding words as conditioned signals, the author says, "in the normal person the word 'sunray' has less effect than the sun ray itself; the letter of a beloved wife makes a weaker impression than her presence." Apropos of consciousness, "the elaborated conditioned reflexes do not always come into consciousness but may be conscious or purely automatic. The conceptions of the conditioned reflex as a fundamental function of the cortex is therefore broader than the conception of the conscious psychic occurrence. It includes every neuropsychic cortical reaction, irrespective of its nature. Thus we have an objective foundation also for those phenomena which Freud calls unconsciousness. The statement that we know nothing of the physical character of latent thoughts is erroneous. We have a real physiologic mechanism at the basis of latent thoughts, which finds its expression in the conditioned process. The difference between the manifest and the latent preconscious phenomenon is that the former occurs in the region of optimal excitability, the latter in an area of decreased excitability" (p. 135).

Suppression is also explained and illustrated diagrammatically on the principle of irradiation and induction. "In most cases the pathologic symptoms develop so that the induced excitation of one region occurs simultaneously with the irradiated inhibition of another, so that excitation of one analyzer and inhibition of another become connected, e.g., pain with paralysis; or the induced excitation meets the irradiated inhibition within one and the same analyzer. Thus there are at the same time hyperalgesia, hypalgesia and analgesia" (p. 147). Unfortunately, Ischlondsky does not say under what different conditions one may expect induction and irradiation.

In the development of neurotic symptoms, three factors play a rôle: (1) The individual experience of the patient, i.e., the cortical connections which have been elaborated by the mechanism of the conditioned reflex and which strongly influence the direction taken by the irradiation and induction of the primary inhibitory focus. (2) The inherited neuropsychic constitution representing conditioned connections of earlier generations. This can determine the form of the neurotic symptoms in exactly the same way as the individual experience. (3) The processes of the phylogenetic development of the organism which determine the inner connections between different territories of the central nervous system and have a marked influence on the form of neurotic symptoms (p. 172). Psychoneuroses are explained as inhibitions brought about by irradiation or induction; dreams as poor differentiations and inhibitions of the original conditioned stimulus in the chain (p. 208 et seq.).

Sublimation is said to be irradiation and induction from the sexual center to another (p. 320). The conditioned reflex is built up on an unconditioned sex reflex. The chivalrous deeds of the knight of the Middle Ages, his self-sacrifice and heroic deeds represent conditioned reflexes of higher orders reaching back to the unconditioned sexual reflexes. These chain conditioned reflexes may be so far

removed that they are hardly recognizable; that which is called sublimation is such a complex of conditioned reflexes of a higher order (p. 324). In sublimation there is a transitory repeating relative inhibition in which the submersion of the positive excitation does not lead to a stable negative fixation, i.e., suppression (p. 327).

The author analyzes Freud's objectivation of the contrast conception brought about by positive induction from an inhibitory process in the cortex of the patient (pp. 225 to 227).

The primary inhibitory focus brought about by suppression, i.e., a breaking down of equilibrium between the excitatory and inhibitory processes, causes lasting irreversible submersion of excitability either by positive induction or by irradiation. In the first case there occur hyperalgesia, tics and hallucinations, and in the second, hypalgesia, analgesia, paresis, anosmia, etc. The character of the symptoms depends on the critical analyzer in which the induction or irradiation of the primal focus occurs. Freud's "conversion" case of Fräulein Elizabeth v. R. is explained as a conflict of excitation and inhibition by positive induction and irradiation involving the pain and sexual centers (p. 255). The case of Frau Emmy v. N. is analogous to the paradoxical state of Pavlov's in which the weak conditioned stimuli have more effect than the strong ones. The paranoid person possesses conditioned reflexes of a higher order built on a highly excitable aggressive defense center (p. 105).

Freud, the author asserts, mixes mysticism and mathematics when he speaks of "conversion" and at the same time the quantity of psychic affect, and also in his differentiation between psychic symptoms of the compulsive neurotic and somatic symptoms of the hysteric. Freud's explanation of conscious and unconscious is said to be less satisfactory than that of the conditioned reflexes on the ground of excitation and inhibition. To Freud he attributes the emancipation from the "degeneration" conception of the French and its replacement by a direct examination of the patient's experience.

The case of Frau Cecilie M. is explained on an entirely different basis from that of Freud's. Ischlondsky maintains that the word "auftreten" has a conditioned connection with the motor area of the patient's cortex, and that "nicht auftreten" represents the stimulus for a negative conditioned reflex or inhibition (p. 277). He cites this case as an example of instances of symbolization that can be successfully explained by objective appearances, "which are in full agreement with the results of animal experimentation (by conditioned reflex methodology)" (p. 277). He agrees with Count Korzybski in thinking that "the development of speech is of great significance for the form of the neurotic symptoms" (p. 284).

The following statements from the concluding chapter illustrate the optimism and perhaps rashness of the author in stating his claim: "As a fundamental element of neuropsychic activity we have in the human being the same process of the conditioned reflex as we have established and can exactly follow in the direct animal experiments. Proceeding from this process and the lawfulness of its course, as well as from its various changes, the whole neuropsychic activity of the human being, in spite of its complexity, can be subjected to direct examination and its mechanics and dynamics discovered. The different expressions of 'thinking,' 'will' and 'feeling' can be explained in their developmental mechanisms" (p. 328). However, this is as yet more a hope of the future than an attainment of the present.

The author states on page 330 that "psychic" influences as very distant conditioned stimuli are usually too fine to deal with in the laboratory, and therefore have given rise to the view that physiology becomes an abstraction when it attempts to deal with them. The assertion that these psychic influences, however, are as objective and obey laws that are as exact as those governing any other function of the organism is in agreement with the conclusions of both the representatives of the conditioned reflex (Pavlov) and the psychobiology (Adolf Meyer) schools of thought.

The second volume concludes thus: "The goal of our research must be the delicate quantitative dependence which comes to have a value in the neuropsychic

(psychobiologic [the term psychobiologic, which already has a definite meaning in this country, is preferable to "neuropsychic" used by Ischlondsky]) phenomena, and the ability to express them in the symbols of mathematics. Here the objective method marks a turning point in the history of human thought . . . [to attain] a precise mathematical knowledge of the whole mental life of the human being. The foregoing work should be the first step along this path" (p. 348).

These two volumes are a welcome addition to the meager authentic literature of conditioned reflexes. The first is of particular value in summarizing, systematizing and explaining Pavlov's work in a more detailed way than is done by Pavlov in many instances. The explanations are aided by diagrams and suggestive examples.

The second volume, dealing with clinical and human material, is of great interest too. Many of the explanations are extremely suggestive, and an ambitious attempt is made to include all of life within the fold of the pavlovian conditioned reflex teaching, by analogy to the laws of excitation, inhibition, irradiation and concentration and induction discovered in dogs by the Pavlov school. While the author gives a clear analysis of the cases he cites, and illustrates admirably the contradictions and mysticism he sees in the freudians, and while his own explanations are plausible and interesting though unproved, it seems a pity that he has not exercised more caution in his applications of the conditioned reflex teaching to human cases. Although his explanations are objective to a degree, much more experimental work is necessary before they can be verified; but until more is known of the laws of irradiation, concentration and induction in the cortex and more can be said as to when and how they occur, under what circumstances, etc., the explanations are more in the nature of carefully thought out analyses and logical analogies than scientific ultimate truths.

Pavlov expresses only the hope that his conditioned reflex methodology will be as useful in human life as in animal cerebral physiology; but whether all life and psychiatry are explainable in the language of the present-day terminology and the very few fundamental laws that Pavlov has discovered or suggested, whether by the simple reflex mechanism advocated by Pavlov or by the conception of segmental and suprasegmental structures as a kind of upper government (Adolf Meyer), and how these conceptions can be brought together remain questions for the future to answer.

The books, in spite of the unrestrained and sometimes unverified optimism they express, are well worth a careful reading by those interested in the broader aspects of biology, medicine and psychology as well as by specialists in these fields.

PERSPEKTIVEN DER SEELENHEILKUNDE. By ARTHUR KRONFELD. Price, 25 marks. Pp. 384. Leipzig: Georg Thieme, 1930.

The desire to get at the final quintessence of the essence of schizophrenia through the very essence of the self of the person runs through this remarkable exposition of a psychology of intentionalism. Subjectivity with a dynamic note, "consciousness as a creative act, as an achievement and as the salvation of selfhood, threatened by anticipated death, sensed and experienced as approaching in the struggle with anxiety or sleep"—that is Kronfeld's fundamental quintessence of schizophrenia, involving all the intentional processes of the person. It is not necessary to search for structural or localizatory corroborations. Kronfeld wants the wise inquirer to know where to stop, lest he might become like Kant's funny man who tries to milk a buck while another holds a sieve for him. "The medical-nosologic point of view is and will be ineffective where we deal with mentality and its modalities and forms." Can this be true?

A closely knit presentation and argument of an intentionalistic self-theory leads to this summary "solution." One cannot help admiring the inner consistency of the effort carried through the 362 large pages of "perspectives of psychopathology." Investigations aiming at the comprehension of the psychic specificity of schizophrenia constitute the goal of this book; "a comprehension of the crazy or paranoetic person now called schizophrenic, viewed from the personal foundations of

his paranoia in his inner life and action, in all his psychic detail structures, together with the world that meets him and as it meets him." The author aims to develop this on ground of a fundamental anthropology on which the normal and psychotic manifestations rest, free from what he considers a blind naturalistic biologism. Psychopathology is to be presented on the basic fact of intentionality and its disorders, seen in the disorders of action, language, drives and volitions, representative imagination and thinking, the delusion formations and the delusional feelings—the upshot of two decades of clinical work and communion with the contemporary workers.

Resting on two previous works ("The Nature of Psychiatric Knowledge," in 1920, and "Psychology in Psychiatry," in 1928), the first chapter brings a discussion of objective psychology and subjective psychology and the second chapter the unity of the person (unity and totality, the Gestalt theory, intentionality and the person). The third chapter discusses the principles of study of the abnormal, leading over to five elaborate chapters on the psychopathology of intentionality (pp. 103 to 322), and the final chapter, the principles of the schizophrenic problems.

The presentation rests everywhere not merely on references to the historical contributors but on a careful statement of the conceptions and systems of these contributors. The book thus represents a valuable document and formulation of a scrupulously intellectualistic analysis, in contrast to the insistent sexualized analysis and final mythologizing of Freud.

The question that torments the American reader of this achievement of German erudition is the quest for the way out, for the return to life and to creative action. Intentionalism without concrete performance in a concrete world of concrete reality constitutes a strangely unmodern search for salvation. It is a forced rationalization of the supposedly irrational and unfathomable, or what one might call the as yet resistant unanalyzed residuum. One might call it respiritualization of the inadequacy feelings facing the structuralist and all those who would like to attain a complete formula. The aphasia problem is turned into an essentially psychopathologic problem to get it out of "that strange mixture of a construction out of somatic and psychic bricks." Catatonic speech becomes the expression of a "total-psychic displacement." A full review of the philosophic trend of German psychiatry is offered in the discussion of volition, craving and compulsion, of "abnormal instinct function," and "abnormal volitional forms"; and the supposed reality of perceived things and their conscious correlates and the problem of perceptual evidence and its falsifications, the ways of the immanent analysis of delusion, the structure of intentional feelings and selfhood and disorders of consciousness of self and delusional feeling. In the discussion of the inner dialectic in Kraepelin's conception of dementia praecox, the author pursues the evaluation of Kahlbaum's rôle with reference to Meyer's evaluation in the historical outline of the discussions of the New York meeting on schizophrenia, the 1896 paper of Freud, Kleist's further development of Wernicke's views, the conception of the psychophrenic split and autism, Berze's "fundamental insufficiency of psychic activity" and the views of the late French psychiatrist, Maurice Mégnard (on "autoconduction" and "subconduction" with the Bergsonian unité psychique and emprise psycho-organique), and the final culmination in the first mentioned conclusion.

The presentation of this self-psychology and self-pathology is consistent and clear, but it raises serious doubts whether the warning of Kant does not hold as much for the too persistent philosopher of the self as for the overeager nosologist or the imaginative organicist. It may be that a frank acceptance of relativity of our methods and formulations keeps us closer to the actualities concerning our control of the facts and our means of presentation and formulation. Which method will lead to the best attacks on the facts as found, and the methods of actual work? There is virtue and actual merit in pushing even pondering to the point of rigidly logical test; but in a field of great difficulty the activity share of pragmatism had best exert itself in close observational and experimental contact with the object rather than with attempts to find salvation in reasoning. The bulk of this study by Kronfeld is a study of the work of Kronfeld and other workers and not to the same extent a study of patients.

INDEX TO VOLUME 26

The star (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, O and S, respectively.

Abscess, brain, surgical treatment of, 887

cold, paralysis of brachial plexus due to, 654

Absinth, effects of absinth on cat, following bilateral adrenalectomy, 651

Accidents, mental causes of child accidents, 1326

Accommodation: See Eye, accommodation

Acid, hydrochloric, microglia and oligodendroglia in experimental intoxication by, 648

hydrochloric, reaction of macroglia and nerve elements to experimental poisoning by, 641

Adamantinoma of craniopharyngeal duct, *905

Adenoma, basophilic, of hypophysis with associated pluriglandular syndrome, report of case, *593

fetal, of hypophysis and dermoid cyst of hypothalamus, 202

Adrenals: See Suprarenals

Adson, A. W.: Raynaud's disease: evidence that it is a type of vasomotor neurosis, *687

Alcohol and central nervous system, 1310

Alcoholism, hemato-encephalic barrier in alcoholic intoxication, 1323

pathologic anatomy of, 628

spinal drainage in alcoholic deliria and other acute alcoholic psychoses, 216

Alexander, F.: Present status of psychoanalysis as a psychologic and therapeutic system, 1108

Schizophrenic psychoses; critical considerations of psychoanalytic treatment, *815

Alexia: See Aphasia, visual

Alpers, B. J.: Adamantinoma of craniopharyngeal duct, *905

Ganglioneuromas of central nervous system, *501

Oligodendrogliomas: clinicopathologic study, *279

Primary fibroblastoma of brain, 1335

Amentia: See Feeblemindedness

American Psychoanalytical Foundation, 1302

Amyloid bodies, occurrence of so-called "amyloid bodies" in ganglion cells of substantia nigra in postencephalitic parkinsonism, 647

Anaphylaxis and Allergy; local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092

Anemia, facial tic in hepatolenticular degeneration with severe secondary anemia resembling pernicious anemia, 419

neurologic complications of pernicious anemia; effects of treatment with liver, *346

pernicious, threatening manifestations of, 1320

pernicious, treatment with hog's stomach, 434

Aneurysm, cerebral, and cortical herniation, *36

congenital, of brain, 858

Angiomas, multiple subcortical venous, 872

Anoxemia, nonsuppurative, nonepidemic encephalitis following labor and in puerperium; report of case probably due to cerebral anoxemia, with a review of literature, *371

Anxiety neuroses, critical review of work of Wilhelm Stekel, *1257

Aphasia, hysterical, contribution to study, 200

visual; nature of literal alexia; contribution to theory of aphasia, 1080

Apparatus, new, for replacement of cerebrospinal fluid by air in encephalography and ventriculography, 1337

Aqueduct of Sylvius, clinical and pathological study of 2 cases of obstruction, 637

Arachnoid, chronic cisternal arachnoiditis producing symptoms of involvement of optic nerves and chiasm, 1074

chronic local arachnoiditis, chiasmal syndorme produced by, 850

fibroblastomas, 640

surgical intervention in myelitis compression caused by arachnoiditis ossificans, 212

Aromatemia and aromaturia from tyrosine in dementia praecox, 633

Aromaturia and aromatemia from tryosine in dementia praecox, 633

Artery, elastic layer in cerebral vessels; studies of new-born and of children, *268

occlusion of right posterior inferior cerebellar artery and right vertebral artery, *396

sylvian, spasm of causing visual hallucinations, 636

Arthus phenomenon, local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092

Astroblastomas of brain, 206

Ataxia, hereditary cerebellar ataxia with interesting encephalographic observations, 2 cases, 666

Atrophy, cerebral muscular atrophy as significant sign of tumor of parietal lobe, 670

of limbs as a sign in involvement of parietal lobe, 237

Atropine, action of atropine in counteracting effects of pituitrin and of pilocarpine injected into cerebral ventricles, 1314

synergistic action of atropine and epinephrine on intrinsic muscles of eye, 649

Ayer, J. B.: Denis-Ayer method for quantitative estimation of protein in cerebrospinal fluid, *1038

Bárány test: See Ear, internal

Bassoe, P.: Familial disease related to Merzbacher-Pelizaeus disease, 226

Klippel-Feil syndrome, 1101

Left hemihypertrophy; reexamination after 20 years, 881

Behavior, Freud's "The discomforts of civilization," 1316

problems, some principles in treatment, 197

Bennett, A. E.: Cerebral aneurysm and cortical herniation, *36

Birth, cerebral birth palsies, contribution to pathology with report of hitherto undescribed form, *524

Bjerrum, sensitive methods for detection of bjerrum and other scotomas, 645

Bleuler, M.: Schizophrenia; review of work of Eugen Bleuler, *610

Blindness, case study in deaf-blindness, 416

Blood and cerebrospinal fluid barrier, effect of some exogenic factors on, 208

and cerebrospinal fluid barrier in manic-depressive psychosis; ratios of distribution of bromide, calcium, sugar and chlorides, *829

calcium; hypocalcemia in new familial malady characterized by congenital cataract and an arrest of somato-neuro-psychic development, 854

calcium in blood and urine of patients with dementia praecox, 1317

cerebrospinal fluid and serum chlorides in meningitis, 450

changes in alkali reserve of blood plasma, of urinary hydrogen ion concentration, and of frequency of convulsive seizures following administration of anticonvulsive drugs and calcium chloride in epileptic persons, 1314

circulation; cerebral circulation; cerebral blood flow and vasomotor response of minute vessels of human brain to histamine, *737

circulation; cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of mixture of carbon dioxide and oxygen, *731

circulation; cerebral circulation; effect of mental work, *725

circulation; cerebral circulation; respiratory quotient of brain and of extremities in man, *719

increase of non-protein nitrogen and decrease of chlorides in blood following vomiting of gastric crises, 865

pressure during hyperventilation and during epileptic fit, 432

pressure, high; hypertension in relation to blood vessels of medulla oblongata, 853

sugar, hyperglycemia in hypopituitarism with glandular treatment, 656

vessels, cerebral anastomoses of, 1070

Blood-letting, mechanism of action of blood-letting on metabolism of water and salts, 1079

Bohrod, M. G.: Encephalitis with unusually high eosinophilia, *1251

Book Reviews:

Adrenals; M. A. Goldzieher, 465

Aerzte als Patienten; A. Grotjahn, 904

Because I Stutter; W. Johnson, 684

Beiträge zur Histologie, Pathogenese und Einteilung der arteriosclerotischen Hirnerkrankung; von K. Neubürger, 466

Bodily Changes in Pain, Hunger, Fear and Rage; W. B. Cannon, 903

Climacteric (The Critical Age); G. Maranon, 680

Common Sense of Drinking; R. R. Peabody, 904

Développement mental et l'intelligence, H. Pieron, 685

Book Reviews—Continued

Diagnosis and Treatment of Brain Tumors; E. Sachs, 1116

Diagnostische Bedeutung des Rossolimoschen Reflex bei Erkrankungen des Zentralnervensystems. Eine klinischanatomische Studie; S. Goldflam, 462

Dictionary of Terms Dealing with Disorders of Speech; S. D. Robbins and S. M. Stinchfield, 681

Discovering Ourselves. A View of the Human Mind and How It Works; E. A. Strecker and K. E. Appel, 465

Evolution of Nervous System in Invertebrates, Vertebrates and Man; C. U. Ariëns Kappers, 467

Experiments with Handwriting; R. Saudek, 686

Freudske psykoanalyse, dens historiske bakgrunn; R. Vogt, 245

Gestalt Psychologie; W. Kohler, 902

Guidance of Mental Growth in Infant and Child; Gesell, 463

Handwörterbuch der medizinischen Psychologie; K. Birnbaum, 903

Handwörterbuch der psychischen Hygiene und der psychiatrischen Fürsorge; O. Bumke, G. Kolb, H. Roemer and E. Kahn, 1118

Jenseits der Seele: Die Scheinwissenschaften in kritischer Betrachtung, M. Dessoir, 1117

Lehrbuch der allgemeinen Physiologie; E. Gellhorn, 1117

Leitfaden der psychischen Hygiene; E. Stransky, 1117

Matrix of the Mind; F. W. Jones and S. D. Porteus, 466

Meaning of Psychoanalysis; M. W. Peck, 686

Mental Aspects of Stammering; C. S. Bluemel, 683

Movements of the Eyes in Reading; M. D. Vernon, 244

Neuropsyche und Hirnrinde; N. E. Ischlondsky, 1361

No Need to Stammer; J. St. J. Rumsey, 682

Parents and the Pre-School Child; W. E. Blatz and H. Bott, 467

Pathologie der Dementia praecox. Gastrointestinale Störungen, ihre klinische und ätiologische Bedeutung, P. J. Reiter, 897

Perspektiven der Seelenheilkunde; A. Kronfeld, 1365

Pflege der Gemüts- und Geisteskranken; W. Morgenthaler, 245

Practique de l'ionisation. Applications medico-chirurgicales; P. Rousseau and P. Nyer, 904

Problematik der Sprachheilschule in ihrer geschichtlichen Entwicklung; K. Hansen, 1113

Psychoanalyse; S. Freud, 686

Psychanalyse im Dienste der Erziehung; O. Pfister, 904

Psychological Factors in Pastoral Treatment of Scruples; J. J. Mullen, 684

Psychologie der Vorpubertät; H. Vorwahl, 1118

Psychology of the Common Branches; W. H. Pyle, 468

Rachithermométrie Humaine: Recherches thermoélectriques; P. Schiff, 686

BOOK REVIEWS—Continued

Sciatique clinique-thérapeutique; J. A. Chavany, 468

Spezielle Chirurgie der Gehirnkrankheiten. (Volume 48 of Neue Deutsche Chirurgie.) Volume I; F. Krause, 464

Stigmatisierte Therese Neumann von Konnersreuth; F. Gerlich, 900

Symbolic Process and Its Integration in Children; J. F. Markey, 685

Treatment of Behavior Disorders Following Encephalitis; E. D. Bond and K. E. Appel, 1115

Treatment of Epilepsy; F. B. Talbot, 246

Treatment of Schizophrenia; L. E. Hinsie, 243

Tumeurs cérébrales. Leurs Manifestations—Leur traitement chirurgical; T. de Martel and J. Guillaume, 461

Umerziehung: Die heilpädagogische Behandlung schwererziehbarer, entgeleister und stotternder Kinder und Jugendlicher; K. C. Rothe, 680

Brachial Plexus, paralysis due to a cold abscess, 654

traumatic lesion with symptoms simulating cervical rib, 1085

Brain: See also Arachnoid; Cerebellum; Hypothalmus; Medulla Oblongata; Meninges; etc.

abscess as otologist's problem, 650

abscess, surgical treatment of, 887

anastomoses of cerebral blood vessels, 1070

astroblastomas of, 206

atrophy; clinicopathologic study of Pick's atrophy, 417

atrophy of limbs as a sign in involvement of parietal lobe, 237

cerebral aneurysm and cortical herniation, *36

certain fundamental cerebral signs and symptoms and their response to dehydration, 452

circulation; cerebral blood flow and vasomotor response of minute vessels of human brain to histamine, *737

circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of mixture of carbon dioxide and oxygen, *731

circulation: effect of mental work, *725

circulation; respiratory quotient of brain and of extremities in man, *719

dilatation of ventricle of septum pellucidum, 198

disturbances of speech and praxia in organic lesions of, 1102

edema and neutralizing action of brain in various solutions, 209

elastic layer in cerebral vessels; studies of new-born and of children, *268

encephalographic studies in cryptogenic epilepsy, *115

encephalography in cases with fixed lesions of brain, 433

encephalography, indications and contraindications of, 205

encephalography; new apparatus for replacement of cerebrospinal fluid by air in encephalography and ventriculography, 1337

encephalography, problem of congenital mental defects; encephalographic observations in congenital and early acquired feeblemindedness, 427

Brain—Continued

experimental studies on corticifugal optic connections in rabbits and apes, 1065

fibroblastoma, primary, 1335

fracture of skull with injury of brain: diagnosis of laceration of orbital surface of frontal lobes, *583

glioma in fourth venticle of prematurely born infant, *1234

von Graefe's sign, a symptom of cerebral localization, 415

gumma of, 864

hemorrhage due to trauma, 1078

injuries during war, 647

intratract fibers and function-bearing systems of floor of third ventricle, 421

lesions in electric shock: histopathology of different types of electric shock on mammalian brains, 1075

lipoids as an index of brain development, value of, 646

local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092

localization of function: effects of fragmentary and complete extirpation of cerebellum in cat; preliminary report on cerebellar localization, *1

localization of function; forced grasping and groping, *600

localization of function: mass responsiveness in central nervous system, *141

medullo-epithelioma of brain with metastasis to head, neck and thorax; report of case, 674

multiple subcortical venous angiomas, 872

nonsuppurative, nonepidemic encephalitis following labor and in puerperium; report of case probably due to cerebral anoxemia, *371

pathologic neurophysiology of a puppy following removal of a hemisphere, 201

symmetrical confluent lesions in frontal lobes in Wilson-pseudosclerosis symptom-complex, 1084

syphilis, an uncommon case of, 1325

tumor, cerebral muscular atrophy as significant sign of tumor of parietal lobe, 670

tumor, localizing diagnosis in brain tumor: phenomena that may be misleading, 651

tumor of parietal lobe, 1342

tumors of quadrigeminate plate, 1067

tumors, 2 cases of tumor of posterior cranial fossa causing visual hallucinations, 652

ventriculography; indications and contraindications of, 205

ventriculography; new apparatus for replacement of cerebrospinal fluid by air in, 1337

wounds, investigations and observations of brain wounds in new-born animals, 1083

Breast cancer, chordotomy of second cervical segment for relief from pain due to recurrent carcinoma of breast, 443

Brock, S.: Dermoid overlying cerebellar vermis, with review of literature on intracranial dermoids, 1089

Dystrophic dysgraphia, 440

Torticollis and righting reflexes and tonic reflexes of neck (Magnus), 441

Bromide: blood-cerebrospinal fluid barrier in manic-depressive psychosis; ratios of distribution of bromide, calcium, sugar and chlorides, *829

Brown, G. E.: Raynaud's disease; evidence that it is a type of vasomotor neurosis, *687

Brown-Séquard syndrome of traumatic origin, 1072

Bubble technic to increase efficiency of lumbar sac medication, *1058

Bulbocapnine, comparative study of action of bulbocapnine and some other drugs in producing catatonic states, 210

investigations of action of bulbocapnine in man, 1312

Caffeine, effect of caffeine on cerebrospinal fluid pressure, 1327

Calcium: blood-cerebrospinal fluid barrier in manic-depressive psychosis; ratios of distribution of bromide, calcium, sugar and chlorides, *829

chloride; changes in alkali reserve of blood plasma, of urinary hydrogen ion concentration, and of frequency of convulsive seizures following administration of anticonvulsive drugs and calcium chloride in epileptic persons, 1314

in blood and urine of patients with dementia praecox, 1317

investigation of anticonvulsive power of calcium alone or associated with parathyroid or irradiated ergosterol in epileptic persons, 646

Camphor, monobromated: a standardized convulsant, *156

Canavan, M. M.: Glioma in fourth ventricle of prematurely born infant, *1234

Cancer, chordotomy of second cervical segment for relief from pain due to recurrent carcinoma of breast, 443

pathology and symptomatology of metastasis of carcinoma to central nervous system, 429

Carbohydrate metabolism in mongolian idiots as evidence of endocrine dysfunction, 649

Carbon bisulphide poisoning, neurologic and psychic phenomena following, 430

dioxide; cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of mixture of carbon dioxide and oxygen, *731

dioxide, effects of inhalation of carbon dioxide and oxygen, and of intravenous sodium amytal on certain neuropsychiatric conditions, 644

disulphide, parkinsonism due to poisoning by, 205

monoxide poisoning and central nervous system, 849

monoxide poisoning, gas poisoning with a dystonic fragment, 443

monoxide poisoning; symptomatic parkinsonism following, 1315

Carmichael, H. T.: Squamous epithelial rests in hypophysis cerebri, *966

Cataplexy, laryngeal vertigo and its relation to cataplexy, 446

Cataract, new familial malady characterized by a congenital cataract and an arrest of somato-neuro-psychic development, 854

Catatonia: See Dementia Praecox

Causalgia: See under Neuralgia

Cave, H. A.: Narcolepsy, *50

Cerebellum, atrophy; 2 cases with moving pictures and pathologic specimens, 677

developmental disturbances of Purkinje neurons, 426

effects of fragmentary and complete extirpation of cerebellum in cat: preliminary report on cerebellar localization, *1

localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 184

localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 186

tumors, 875

Cerebrospinal Fluid, anatomic variations of cranial venous sinuses: their relation to effect of jugular compression in lumbar manometric tests, *801

and serum chlorides in meningitis, 450

blood-cerebrospinal fluid barrier, effect of some exogenic factors on, 208

blood-cerebrospinal fluid barrier in manic-depressive psychosis: ratios of distribution of bromide, calcium, sugar and chlorides, *829

bubble technic to increase efficiency of lumbar sac medication, *1058

cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of mixture of carbon dioxide and oxygen, *731

effect of caffeine on cerebrospinal fluid pressure, 1327

internal jugular venous pressure and its relationship to pressure of spinal fluid, 892

of premature infants, 216

protein; Denis-Ayer method for quantitative estimation of protein in spinal fluid, *1038

Takata-Ara test in 400 cases, results of, 893

Cerebrum: See Brain

Cestan-Chenais bulbar syndrome, indistinct type of: paralysis of ninth, tenth and eleventh cranial nerves and slight left hemiparesis, 635

Chicago Academy of Criminology, 1301

Chickenpox, nonsuppurative encephalomyelitis accompanying chickenpox, *322

Children, child of very superior intelligence as a special problem in social adjustment, 1085

new familial malady characterized by congenital cataract and arrest of somato-neuro-psychic development, 884

Chlorides, blood-cerebrospinal fluid barrier in manic-depressive psychosis: ratios of distribution of bromide, calcium sugar and chloride, *829

Chordotomy: See Spinal Cord, surgery

Chorea, chronic chorea and its relation to striatum, 1068

clinical value of a new reflex in, 863

Huntington's, 863

Chorio-epithelioma, report of a pathologic specimen of chorio-epithelioma malignum, 224

Choroid plexus as a dialyzing membrane; observations in experimental hydrocephalus, *496

Clarke, E. K.: Abnormal personalities, 1332

Claude's inferior syndrome of red nucleus associated with Parinaud's syndrome, 1319

Climacteric: See Menopause

Climate, does climate affect human conception rate? 864

Cobb, S.: Cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalations of mixture of carbon dioxide and oxygen, *731

Cohen, P.: Effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226

Colitis, ulcerative, brief psychological analysis of case of, 204

Color-blindness, hemiachromatopsia in hemianopic macular scotoma, 859

Conception, does climate affect human conception rate? 864

Convulsions, certain fundamental cerebral signs and symptoms and their response to dehydration, 454

changes in alkali reserve of blood plasma, of urinary hydrogen ion concentration, and of frequency of convulsive seizures following administration of anticonvulsive drugs and calcium chloride in epileptic persons, 1314

convulsive state with unusual pathologic conditions, 451

effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226

Coombs, H. C.: Monobromated camphor; a standardized convulsant, *156

Cooper, M. J.: Primary tumor of gasserian ganglion, 1357

Corpus callosum, tumor of posterior corpus callosum, 441

ponto-bulbare, dystopias of, 1081

Couch, F. H.: Optic nystagmus; psychologic conditions, *23

Craig, W. McK.: Multiple tumors of skull simulating osteomyelitis, *393

Craniopharyngeal duct, adamantinoma of, *905 pouch tumors, 420

Cranium, anatomic variations of cranial venous sinuses: their relation to effect of jugular compression in lumbar manometric tests, *801

dermoid overlying cerebellar vermis, with a review of literature on intracranial dermoids, 1089

exophthalmos associated with diabetes insipidus and large defects in bones of skull, 644

fracture of skull with injury of brain; diagnosis of laceration of orbital surface of frontal lobes, *583

multiple tumors of skull simulating osteomyelitis, *393

nontraumatic osteomyelitis of flat bones of skull, 449

unilateral paralytic syndrome of last 7 cranial nerves and cervical sympathetic from a tumor destroying cranial base, 1073

Crime, criteria of responsibility, 857
psychiatric aspects of, 1328, 1329

Criminal feebleminded, 853
who are criminal insane, 215

Cuneate nucleus, 630

Currier, F. P.: Forced grasping and groping, *600

Cyst, gliomatous cyst of spinal cord in a boy 16 years of age, 678

Daffinee, R. W.: Results of Takata-Ara test in 400 cases; preliminary report, 893

Dailey, M. E.: Cerebrospinal fluid and serum chlorides in meningitis, 450

Denis-Ayer method for quantitative estimation of protein in cerebrospinal fluid, *1038

Davidoff, L. M.: Effects of fragmentary and complete extirpation of cerebellum in cat; preliminary report on cerebellar localization, *1

Local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092

Davidson, H. A.: Plantar reflexes in normal adults, *1027

Davis, D. B.: Forced grasping and groping, *600

Davis, T. K.: Pellagra with neurologic manifestations, 438

Davison, C.: Intramedullary neoplasm of cord with hematosyringomyelia, 873

Multiple subcortical venous angiomas, 872

Subacute combined degeneration of cord; changes following liver therapy; histopathologic study, *1195

Deafness, case study in deaf-blindness, 416

Deglutition, disturbances of deglutition in neuropathology, 215

Dehydration, certain fundamental cerebral signs and symptoms and their response to dehydration, 452

Delinquency, behavior problems in children with special reference to, 216

Delirium Tremens, importance of disturbances of liver function in alcoholic delirium and a causal method of treatment, 1083

spinal drainage in alcoholic deliria and other acute alcoholic psychoses, 216

Dementia Paralytica: See Paralysis, general

Dementia Praecox, aromatemia and aromaturia from tyrosine in, 633

calcium in blood and urine of patients with, 1317

comparative study of action of bulbocapnine and some other drugs in producing catatonic states, 210

hepatic function in amentia and dementia praecox, 423

physiogenic and psychogenic in schizophrenia, 864

review of work of Eugen Bleuler on schizophrenia, *610

schizophrenic psychoses: critical considerations of psychoanalytic treatment, *815

study of some schizoid children, 650

unconditioned and conditioned reactions to pain in schizophrenia, 213

Demoor, sign of; phenomenon of false estimation of weights in mentally defective, 648

Denis-Ayer method for quantitative estimation of protein in cerebrospinal fluid, *1038

Depression: See Melancholia

Dermoid cyst, fetal adenoma of hypophysis and dermoid cyst of hypothalamus, 202

overlying cerebellar vermis, with a review of literature on intracranial dermoids, 1089

Diabetes, antagonistic biochemical mechanisms in diabetes and epilepsy, 1336

insipidus, exophthalmos associated with diabetes insipidus and large defects in bones of skull, 644

Diathermy in fever therapy of dementia paralytica, 662

Diphtheria, postdiphtheric levogyric paralysis of eyes, 208

Dodge, R.: Optic nystagmus; psychologic conditions, *23

Dorsey, J. M.: Mass responsiveness in central nervous system, *141

Drug Addiction, psychoses due to, 216

report of Mayor's committee on drug addiction to Commissioner of Correction, New York City, 189

Duane, W., Jr.: Polycythemia vera, 231

Dura, endothelioma of, 640

Dysgraphia, dystrophic dysgraphia, 440

Dysinsulinism, rôle of dysinsulinism in epilepsy syndrome, 868

Dystonia: See under Muscle

Dystrophy, heart rate in progressive muscular dystrophy, 433

Ear, influence of columella on formation of lamina propria of tympanic membrane, 860

internal: localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 184, 186

internal: localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 186

Parinaud's syndrome with labyrinthine disturbances; physiopathologic mechanism of this syndrome, 198

report on experiments on rabbits with a view to determining time taken by reaction of eye on mechanical or galvanic irritation of labyrinth of ear, 428

Ectodermoses, congenital ectodermoses (neurocutaneous syndromes) in epileptic patients, *1145

Edwards, E. A.: Anatomic variations of cranial venous sinuses; their relation to effect of jugular compression in lumbar manometric tests, *801

Electric blanket, fever treatment for dementia paralytica by means of diathermy and electric blanket, 662

resistance, high electrical resistance of skin of new-born infants and its significance, 437

shock, lesions of brain in: histopathology of different types of electric shock on mammalian brains, 1075

stimuli for posture and movement, 1322

Embolism and thrombosis, prolonged direct observations of phenomena in pial vessels of living cat, 859

Emotions, neurasthenia as a manifestation of emotional disturbances, 435

Encephalitis: See also Encephalomyelitis

clinical and pathological study of 3 cases of, 429

clonic oculogyric crises in epidemic, 1348

occasional fulminating course of, *607

late cochleovestibular manifestations of epidemic encephalitis, 1060

nonsuppurative, nonepidemic encephalitis following labor and in puerperium; report of case probably due to cerebral anoxemia, with review of literature, *371

Encephalitis—Continued

permanent conjugate deviation of eyes in epidemic encephalitis with contralateral loss of postural reflex and muscular hypotonia: a peculiar syndrome, 206

unilateral myoclonic movements probably of encephalitic origin, 668

with unusually high eosinophilia, *1251

Encephalography: See under Brain

Encephalomyelitis, nonsuppurative encephalomyelitis accompanying chickenpox, *322

Endarteritis, productive-degenerative form of endarteritis of small pial vessels: report of case showing unusual clinical and histologic features, *993

Endocrine Glands, basophilic adenoma of hypophysis with associated pluriglandular syndrome, report of case, *593

dysfunction; carbohydrate metabolism in mongolian idiots as evidence of endocrine dysfunction, 649

endocrinologic investigations in epileptics, 424

pluriglandular compensatory syndrome, 656

Endothelioma, dural, 640

meningeal fibroblastomas (dural endotheliomas, meningiomas, arachnoid fibroblastomas), 640

Epilepsy, antagonistic biochemical mechanisms in diabetes and epilepsy, 1336

attacks 16 years after trauma of head; operation, 1087

biological and serological methods of diagnosis, 427, 860

blood pressure during hyperventilation and during epileptic fit, 432

changes in alkali reserve of blood plasma, of urinary hydrogen ion concentration, and of frequency of convulsive seizures following administration of anticonvulsive drugs and calcium chloride in epileptic persons, 1314

congenital ectodermoses (neurocutaneous syndromes) in epileptic patients, *1145

cryptogenic, encephalographic studies in, *115

endocrinologic investigations in, 424

induction of sleep in epileptic persons, *131

influence of diet low in pellagra-preventive factor, 634

investigation of anticonvulsive power of calcium alone or associated with parathyroid or irradiated ergosterol in, 646

mechanism of epileptic seizures: some data favoring hypothesis of vegetative epileptogenous center in diencephalic region, 1071

of angiospastic variety in monozygotic twins, 886

relation of time of day, sleep and other factors to incidence of epileptic seizures, 639

results from use of ketogenic diet and ketogenic diet with water restriction in series of epileptics, 847

rôle of dysinsulinism in epilepsy syndrome, 868

traumatic epilepsy treated by excision of cerebral cortex according to Penfield-Foerster method, 233

Epinephrine: See Suprarenal preparation

Epithelial rests; squamous epithelial rests in hypophysis cerebri, *966

Epithelioma, medulloepithelioma of brain with metastasis to head, neck and thorax: report of case, 674

Ergosterol, investigation of anticonvulsive power of calcium alone or associated with parathyroid or irradiated ergosterol in epileptic persons, 646

Exophthalmos associated with diabetes insipidus and large defects in bones of skull, 644

enormous mucocele of frontal sinus with exophthalmos and hyperostosis of orbital bone, 654

unilateral exophthalmos following administration of thyroid extract, 866

Eye: See also under special structures of eyes, i. e., Optic Chiasm; Retina; etc.

accommodation, weakness of, 422

effect of experimental excision of one eye on development of optic lobe and opticus layer and larvae of tree-frog (Hyla regilla); effect on cell size and differentiation of cell processes, 215

effect of labyrinthine and cortical stimulation on position of eyes following section of posterior longitudinal bundle, 1086

horizontal nystagmus with changing direction according to suppression of vision of one or other eye; tonic and kinetic disturbances of eyes following traumatism in syphilitic, 190

influence of transplanted eyes on development of spinal nerves in Amblystoma punctatum, 213

intra-ocular pressure; physico-chemical factors controlling intra-ocular pressure, 1077

mechanism of some convulsive movements of orbicularis and of face, 866

movements, 192

movements; central nervous system control of ocular movements and disturbance of this mechanism, 191

movements; Claude's inferior syndrome of red nucleus associated with Parinaud's syndrome, 1319

movements; Parinaud's syndrome appearing suddenly in course of Parkinson's disease, 634

movements: Parinaud's syndrome with labyrinthine disturbances; physiopathologic mechanism of this syndrome, 198

muscle, inferior oblique hyperfunction of, 640

paralysis; examination of peripheral oculomotor paralysis, 1308

paralysis of lateral movements of eyes and dissociated nystagmus in multiple sclerosis, 409

paralysis of lateral movements from pontile lesion; study of oculogyric pathways, 402

paralysis of movements of laterality of eyes, 2 anatomicoclinical observations, 405

permanent conjugate deviation of eyes in epidemic encephalitis with contralateral loss of postural reflex and muscular hypotonia: a peculiar syndrome, 206

postdiphtheric levogyric paralysis of, 208

reflex transmission of stimuli from one eye to other, 430

report on experiments on rabbits with view to determining time taken by reaction of eye on mechanical or galvanic irritation of labyrinth of ear, 428

synergistic action of atropine and epinephrine on intrinsic muscles of, 649

Face, causalgia, 1076

mechanism of some convulsive movements of orbicularis and of, 866

Paralysis: See under Paralysis

Fay, T.: Certain fundamental cerebral signs and symptoms and their response to dehydration, 452

Medullo-epithelioma of brain with metastasis to head, neck and thorax; report of case, 674

Feebleminded, criminal, 853

congenital problem of feeblemindedness, 211

hepatic function in amentia and dementia praecox, 423

necessity for central registration of mental defectives, 861

neurologic and etiologic study on 1000 mental defectives, 857

phenomenon of false estimation of weights in mentally defective, 648

problem of congenital mental defects; encephalographic observations in congenital and early acquired feeblemindedness, 427

Ferraro, A.: Effects of fragmentary and complete extirpation of cerebellum in cat; preliminary report on cerebellar localization, *1

Fever Treatment: See also Malaria, therapeutic

for dementia paralytica by means of diathermy and electric blanket, 662

use of sulphur for production of fever, *102

Fibroblastoma, meningeal, 640

primary, of brain, 1335

Finger-prints; palm and sole patterns in identical twins, 1352

Finley, K. H.: Neuro-anatomy in respiratory failure; report of 2 cases, *754

Foramen, respiratory sequelae in a case with syndrome of posterior lacerated foramen, 15 years after traumatism, 203

Fox, J. C., Jr.: Optic nystagmus; psychologic conditions, *23

Frank, R. T.: Hormonal causes of premenstrual tension, *1053

Frazier, C. H.: Adamantinoma of craniopharyngeal duct, *905

Freedom, L.: Cerebral birth palsies; contribution to their pathology with a report of hitherto undescribed form, *524

Freeman, W.: Cerebellar atrophy; 2 cases with moving pictures and pathologic specimens, 677

Fremont-Smith, F.: Cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of a mixture of carbon dioxide and oxygen, *731

Cerebrospinal fluid and serum chlorides in meningitis, 450

Denis-Ayer method for quantitative estimation of protein in cerebrospinal fluid, *1038

Freud's "discomforts of civilization," 1316

theory of instinct and other psycho-biological theories, 629

Friedman, E. D.: Kümmell's spondylitis, 439

Frontal sinus, enormous mucocele with exophthalmos and hyperostosis of orbital bone, 654

Galvanic current, influence of galvanic current on regeneration of injured nerves, 204

skin-reflex: further aspects in psychopathologic groups, *146; correction, 400

Ganglia, effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226

Ganglioneuroma of central nervous system, *501 of retroperitoneal origin, 212

Gasserian ganglion, primary tumor of, 1357

Gault, R. H.: Experiments on use of sense of touch in relation to language, 1101

Gerard, R. W.: Metabolism of nerves and problem of degeneration, 884

Regenerative possibilities of central nervous system, *469

Gestalt psychology, social implication of, 653

Ginger Paralysis: See under Paralysis

Glia: See Neuroglia

Glioma, case of gliomatous cyst of spinal cord in a boy, 678

classification of gliomas and neuroglia cell types, *745, 876

extension of glioma (retinoblastoma) into optic nerve, 642

in fourth ventricle of prematurely born infant, *1234

Goiter and iodine deficiency; influence of diet poor in iodine on thyroid in white rats, 852

exophthalmic, iodine in comparison of effect of ethyl iodide and potassium iodide with that of Lugol's solution, 1327

exophthalmic; nature of Graves' disease, 431

exophthalmic, prolonged treatment by iodine alone, 437

exophthalmic, thyrotoxicosis following subtotal thyroidectomy for, 214

Goodyear, A. F.: Encephalitis with unusually high eosinophilia, *1251

Gordon, A.: Unilateral myoclonic movements probably of encephalitic origin, 668

Gradenigo's syndrome; anatomic aspects, 412

von Graefe's sign, a symptom of cerebral localization, 415

Grant, F. C.: Ganglioneuromas of central nervous system, *501

Primary fibroblastoma of brain, 1335

Surgical treatment of abscess of brain, 887

Grasping, forced grasping and frontal lobe, 1069

forced grasping and groping, *600

reflex in new-born monkey, *784

Graves' Disease: See Goiter, exophthalmic

Grinker, R. R.: Regenerative possibilities of central nervous system, *469

Guanidine, microglia and oligodendroglia in experimental intoxication by, 648

reaction of macroglia and nerve elements to experimental poisoning by, 641

Gumma of brain, 864

Gurdjian, E. S.: Fracture of skull with injury of brain; diagnosis of laceration of orbital surface of frontal lobes, *583

Guthrie, R. H.: Congenital ectodermoses (neurocutaneous syndromes) in epileptic patients, *1145

Gynecology, psychotherapy in, 1086

Hadden, S. B.: Incipient parkinsonism; group of objective symptoms of value in its early recognition, *392

Neuritis and multiple neuritis following serum therapy, 1353

Two cases of hereditary cerebellar ataxia with interesting encephalographic observations, 666

Hallucinations in a visual semifield from spasm of sylvian artery, 636

visual, tumor of posterior cranial fossa causing, 2 cases, 652

Handwriting, time and lineage factors of handwriting; experimental study based on specimens secured from 200 normal persons and from 148 persons with dementia paralytica, *333

Harris, T. H.: Occlusion of right posterior inferior cerebellar artery and right vertebral artery, *396

Harrow, R.: Traumatic epilepsy treated by excision of cerebral cortex according to Penfield-Foerster method, 233

Hassin, G. B.: Spasmodic torticollis, *1043

Hauser, A.: Occlusion of right posterior inferior cerebellar artery and right vertebral artery, *396

Haven, H. A.: Chorio-epithelioma malignum, 224

Head murmers, 1327

Headache, certain fundamental cerebral signs and symptoms and their response to dehydration, 452

Healy, W.: Abnormal personalities, 1332

Hearing, status of tests of hearing with report of speech interpretation test, 436

Heart, functional reactions in embryonic heart accompanying ingrowth and development of vagus innervation, 210

pain, 434

rate in progressive muscular dystrophy, 433

Hebephrenia, hebephrenic syndrome, 217

Hemato-Encephalic Barrier: See Meninges, permeability

Hematomyelia, 1349

Hematosyringomyelia: See Syringomyelia

Hemiachromatopsia: See Color-blindness

Hemianopia, anisocoria in bitemporal hemianopia evolved from one eye, 1325

binasal, case of, 638

Hemiballismus, contribution to knowledge of, 1318

Hemihypertrophy: See under Hypertrophy

Hemsath, F. A.: Glioma in fourth ventricle of prematurely born infant, *1234

Herpes zoster oticus, 652

sodium iodide in, 865

solution of pituitary in, 653

Hinsey, J. C.: Contralateral flexor reflex, rebound phenomena, co-contraction and reciprocal innervation in spinal and in decerebrate cats, *247

Hinsie, L. E.: A hebephrenic syndrome, 217

Histamine, cerebral circulation; cerebral blood flow and vasomotor response of minute vessels of human brain to, *737

microglia and oligodendroglia in experimental intoxication by, 648

reaction of macroglia and nerve elements to experimental poisoning by, 641

Hodgkin's Disease: See Lymphogranuloma

Hoen, T. I.: Choroid plexus as a dialyzing membrane, observations in experimental hydrocephalus, *496

Holloway, T. B.: Moving pictures of visual fields, 242

Holt, E. K.: Psychiatric aspects of crime, 1329

Hydrocephalus, choroid plexus as a dialyzing membrane, observations in experimental hydrocephalus, *496

Hyperinsulinism: See Pancreas disease

Hypertonia, investigation on origin of early hypertonia and of neck reflexes of Magnus and DeKleyn, 631

Hypertrophy, left hemihypertrophy, reexamination after 20 years, 881

Hypocalcemia: See Blood calcium

Hypophysis: See Pituitary Body

Hypothalamus: See also Pituitary Body

disorders induced by injury to, 658

fetal adenoma of hypophysis and dermoid cyst of, 202

structure and function of cells of tuber cinereum, 643

Hyslop, G. H.: Tumor of posterior corpus callosum, 441

Hysteria, approach to study of, 1324

Idiocy, mongolian, carbohydrate metabolism in mongolian idiots as evidence of endocrine dysfunction, 649

Insane, who are criminal insane, 215

Insanity, incidence of syphilis in insanity, 437

Instinct, Freud's theory of instinct and other psycho-biological theories, 629

Intelligence, researches into forms of intelligence, 435

Tests: See Mental tests

Intestine, worms as etiologic factor in multiple sclerosis, 866

Iodine deficiency and goiter; influence of diet poor in iodine on thyroid gland in white rats, 852

in exophthalmic goiter: comparison of effect of ethyl iodide and potassium iodide with that of Lugol's solution, 1327

prolonged treatment of exophthalmic goiter by iodine alone, 437

Iodobismitol in neurosyphilis, *1220

"Jake" Paralysis: See under Paralysis

Jamaica Ginger, paralysis due to: See under Paralysis

Johnson, C. A.: Knee jerk; effects of stimulation of some abdominal viscera on patellar jerk, *162

Kahn Test: See Syphilis, serodiagnosis

Karpman, B.: Anxiety neuroses; critical review of work of Wilhelm Stekel, *1257

Kasanin, J.: Abnormal personalities, 1332

Keegan, J. J.: Cerebral aneurysm and cortical herniation, *36

Kennedy, F.: Dystonia musculorum deformans, 444

Gas poisoning with a dystonic fragment, 443

Kenyon, J. H.: Hyperglycemia in hypopituitarism with glandular treatment, 656

Ketosis in sea-sickness, 865

Kinder, E. F.: Galvanic skin-reflex; further aspects in psychopathologic groups, *146; correction, 400

Klauder, J. V.: Demonstration of Wechselmann lumbar puncture needles, 230

Klenke, D.: Dermoid overlying cerebellar vermis, with review of literature on intracranial dermoids, 1089

Klippel-Feil syndrome, 1101

Knee Jerk and its variation; indication for sympathetic ramisection or trunk section, 214

effects of stimulation of some abdominal viscera on patellar jerk, *162

Kuntz, A.: Anatomic basis of sympathectomy, 444

Kwan, S. T.: Oligodendrogliomas; clinicopathologic study, *279

Labor, nonsuppurative, nonepidemic encephalitis following labor and in puerperium; report of case probably due to cerebral anoxemia, with review of literature, *371

Labyrinth: See under Ear

Language, disorders in development of language, 411

experiments on use of sense of touch in relation to, 1101

Larynx, continuous rhythmic movements of palate, pharynx and, *1236

laryngeal vertigo and its relation to cataplexy, 446

Laurence-Biedl syndrome, 655

Lead acetate, reaction of macroglia and nerve elements to experimental poisoning by, 641

microglia and oligodendroglia in experimental intoxication by, 648

Leavitt, F. H.: Juvenile dementia paralytica occurring in third generation of syphilitic family, 665

Palm and sole patterns in identical twins, 1352

Lehrman, P. R.: An initial visit, 1104

Lennox, W. G.: Cerebral circulation; cerebral blood flow and vasomotor response of minute vessels of human brain to histamine, *737

Cerebral circulation; effect of mental work, *725

Cerebral circulation; respiratory quotient of brain and of extremities in man, *719

Lenticular nucleus, pathogenesis of hepatolenticular degeneration, 432

Leonhardt, E.: Cerebral circulation; effect of mental work, *725

Cerebral circulation; respiratory quotient of brain and of extremities in man, *719

Leshin, N.: Continuous rhythmic movements of palate, pharynx and larynx, *1236

Lewis, R.: Hematomyelia, 1349

Light, activating influence of light upon certain aquatic arthropods, 1324

some factors involved in reaction of insects to changes in luminous intensity; shock reactions in Dineutes assimilis, 211

Lillie, R. D.: Histopathology of triorthocresyl phosphate poisoning; etiology of so-called ginger paralysis (third report) *976

Lindemulder, F. G.: Myelitis occurring in primary and in secondary stage of syphilis, *167

Lipoids, value of brain lipoids as an index of brain development, 646

Liver function in amentia and dementia praecox, 423

importance of disturbances of liver function in alcoholic delirium and a causal method of treatment, 1083

pathogenesis of hepatolenticular degeneration, 432

therapy in subacute combined degeneration of cord, *1195

therapy in neurologic complications of pernicious anemia, *346

Loman, J.: Internal jugular venous pressure and its relationship to pressure of cerebrospinal fluid, 892

Low, A. A.: Disturbances of speech and praxia in organic lesions of brain, 1102

Lowenberg, K.: A productive-degenerative form of endarteritis of small pial vessels; report of case showing unusual clinical and histologic features, *993

Luckhardt, A. B.: Knee jerk; effects of stimulation of some abdominal viscera on patellar jerk, *162

Lugol's solution; iodine in exophthalmic goiter: a comparison of effect of ethyl iodide and potassium iodide with that of Lugol's solution, 1327

Lumbar sac medication, bubble technic in, *1058

Lung, peripheral neuritis complicated by massive collapse of lung following tonsillectomy, 212

Lurie, L.: Fever treatment for dementia paralytica by means of diathermy and electric blanket, 662

Lymphogranuloma, spinal cord changes in lymphogranulomatosis, *1009

Mackay, R. P.: Use of sulphur for production of fever, *102

McKinney, J. McD.: Laurence-Biedl syndrome, 655

Macroglia, reaction of macroglia and nerve elements to experimental poisoning by histamine, guanidine, hydrochloric acid, lead acetate and thallium acetate, 641

Macula, Niemann-Pick's disease with cherry-red spots in, 861

Malamud, W.: Blood-cerebrospinal fluid barrier in manic-depressive psychosis; ratios of distribution of bromide, calcium, sugar and chlorides, *829

Malaria therapy, medicolegal complications of, 653

Malingering in persons accused of crime, 3 cases, 447

Manganese poisoning, case of parkinsonism due to, 1335

Mastoiditis, lateral sinus thrombosis complicating masked mastoiditis, 653

Mayer, L. L.: Quantitative measurement of pupillary and light reactions, 1100

Medulla oblongata, hypertension in relation to blood vessels of, 853

Mehrtens, H. G.: Iodobismitol in treatment for neurosyphilis, *1220

Melancholia, study of structure of depressive states; the ambivalent depressions, 407

Meninges, bubble technic to increase efficiency of lumbar sac medication, *1058

meningeal fibroblastomas (dural endotheliomas, meningiomas, arachnoid fibroblastomas), 640

permeability, "permeability quotients" of calcium chloride (total halogens) and bromide and their mutual relations in endogenous mental diseases, 1323

permeability; hemato-encephalic barrier in alcoholic intoxication, 1323

Meningiomas, meningeal fibroblastomas (dural endotheliomas, meningiomas, arachnoid fibroblastomas), 640

Meningitis, cerebrospinal fluid and serum chlorides in meningitis, 450

purulent, cerebral lesions in, *549

Menopause, psychoses in climacteric and involutional periods, 414

Menstruation, hormonal causes of premenstrual tension, *1053

Mental defectives: See Feebleminded

Mental Diseases: See also Insanity; Psychoses; etc.

discrete ocular and labyrinthine signs in subject with mental disturbances, 642

reaction of neuroglia and of nerve cells in toxic mental syndromes, 650

Mental Hygiene, college, approach to, 646

importance of mental hygiene in other departments of medical practice, 652

mental dangers among college students, 651

Mercury poisoning, clinical picture and pathology, 404

Merzbacher-Pelizaeus disease: See under Sclerosis

Metabolism, cerebral circulation; respiratory quotient of brain and of extremities in man, *719

Metamorphosis, amphibian; influence of columella on formation of lamina propria of tympanic membrane, 860

Meyer, A.: August Forel, 1303

Orientations of training and practice in neurology and psychiatry, 218

Microglia: See under Neuroglia

Middleton, W. S.: Occasional fulminating course of encephalitis epidemica, *607

Movement, adequate electrical stimuli for, 1322

constitutional variations of psychomotor functions and their relationship to physique and character, 199

continuous rhythmic movements of palate, pharynx and larynx, *1236

Moving pictures of visual fields, 242

Mucocele, enormous, of frontal sinus with exophthalmos and hyperostosis of orbital bone, 654

Muncie, W.: Rigid personality as a factor in psychoses, *359

Munro, D.: Myelotomy in treatment for syringomyelia, 889

Nontraumatic osteomyelitis of flat bones of skull, 449

Muscle contraction, contralateral flexor reflex, rebound phenomena, co-contraction and reciprocal innervation in spinal and in decerebrate cats, *247

Muscle—Continued
dystonia musculorum deformans, 444
method of exciting incipient movement in weakened and paralyzed muscles, 436
Music, morphologic correlate of musical talent, 431
Myelitis occurring in primary and in secondary stage of syphilis, *167
surgical intervention in myelitis compression caused by arachnoiditis ossificans, 212
transverse, with apoplectiform onset; clinical and pathologic study of myelomalacia, 202
Myelomalacia: See under Spinal Cord
Myerson, A.: Internal jugular venous pressure and its relationship to pressure of cerebrospinal fluid, 892
Three cases of malingering in persons accused of crime, 447
Myoclonus, unilateral myoclonic movements probably of encephalitic origin, 668
Myopathy: See under Muscle
Myxedema, psychosis associated with myxedema, 428

Narcolepsy: See under Sleep
Neck, investigation on origin of early hypertonia and of neck reflexes of Magnus and DeKleyn, 631
Needles, W.: Neurologic complications of pernicious anemia; effects of treatment with liver, *346
Nerve cells, on reaction of neuroglia and nerve cells in toxic mental syndromes, 650
cranial; evolution of syndrome of last four cranial nerves, 193
fibers, cutaneous sensory fibers and sensory conduction, *1122
fibers, structure of, 632
metabolism of nerves and problem of degeneration, 884
neurons of sensory type in ventral roots of man and of other mammals, *791
ninth, tenth and eleventh cranial nerves, paralysis of, 635
oculomotor, humoral effect of stimulation of, 1326
optic; chronic cisternal arachnoiditis producing symptoms of involvement of optic nerves and chiasm, 1074
optic, extension of glioma (retinoblastoma) into, 642
optic, hereditary optic atrophy (Leber's disease), 637
reaction of macroglia and nerve elements to experimental poisoning by histamine, guanidine, hydrochloric acid, lead acetate and thallium acetate, 641
regeneration; influence of galvanic current on regeneration of injured nerves, 204
spinal, influence of transplanted eyes on development of spinal nerves in Amblystoma punctatum, 213
spinal, sensory fibers in, 886
trigeminal, differential section of dorsal root of, 442
tumor of petrous bone of malpighian origin involving dura and cranial nerves, 423
Nerve—Continued
unilateral paralytic syndrome of last 7 cranial nerves and cervical sympathetic from a tumor destroying cranial base, 1073
Nervous System, central, and alcohol, 1310
central, regenerative possibilities of, *469
changes in central nervous system in septic pyemia, 845
characteristics of distribution of diseases in central nervous system, 410
ganglioneuromas of, *501
investigation of central nervous system by polarized light, 209
mass responsiveness in central nervous system, *141
nuclear changes simulating inclusion bodies in dorsal-root ganglion cells, 867
pathology and symptomatology of metastasis of carcinoma to central nervous system, 429
sympathetic; injury and repair within; preganglionic neurons, *485
sympathetic, rationalizing surgery of, 429
syphilis: See Syphilis
Neuralgia, facial causalgia, 1076
facial, treated by retrogasserian neurotomy, 200
trigeminal, radical operations for, 650
trigeminal, treatment with trichlorethylene, 433
Neurasthenia as manifestation of emotional disturbances, 435
Neuritis and multiple neuritis following serum therapy, 1353
optic; papillary edema during pregnancy cured by lumbar puncture, 1082
peripheral, complicated by massive collapse of lung following tonsillectomy, 212
retrobulbar, relation of paranasal sinuses to ocular disorders especially to, 636
retrobulbar; variations in retinal arterial tension following nasal operation, 645
Neurocutaneous syndromes; congenital ectodermoses (neurocutaneous syndromes) in epileptic patients, *1145
Neurofibromatosis, multiple, 653
Neuroglia, classification of gliomas and neuroglia cell types, *745, 876
microglia and oligodendroglia in experimental intoxication by histamine, guanidine, hydrochloric acid, thallium and lead, 648
oligodendrogliomas, *279
reaction of neuroglia and nerve cells in toxic mental syndromes, 650
Neurology, aid in neurologic diagnosis, 210
are neurology and psychiatry separate medical entities? 431
orientations of training and practice in neurology and psychiatry, 218
progress, *1119
Neurons of sensory type in ventral roots of man and of other mammals, *791
Neuropsychiatry, have psychologic concepts a practical value in, 219
Neuroses, anxiety; critical review of work of Wilhelm Stekel, *1257

Neuroses—Continued
complementary neurosis in a married couple, 1107
have psychologic concepts a practical value in neuropsychiatry, 219
neurotic character and the pervert, 1095
Neurosyphilis: See Syphilis
Nielsen, J. M.: Rôle of dysinsulinism in epilepsy syndrome, 868
Niemann-Pick's disease with cherry-red spots in macula, 861
Nose, relation of paranasal sinuses to ocular disorders, especially to retrobulbar neuritis, 636
Notkin, J.: Encephalographic studies in cryptogenic epilepsy, *115
Nucleus, cuneate: See Cuneate nucleus
triangularis: See Cuneate Nucleus
Red: See Tegmental nucleus
Nystagmus, certain reflexes, especially oculocardiac reflex and provoked nystagmus, in case of pathologic sleep, 413
horizontal nystagmus with changing direction according to suppression of vision of one or other eye; tonic and kinetic disturbances of eyes following traumatism in syphilitic, 190
miners', 1077
of ocular origin, 855
optic: psychologic conditions, *23
paralysis of lateral movements of eyes and dissociated nystagmus in multiple sclerosis, 409

Oberndorf, C. P.: Complementary neurosis in a married couple, 1107
OBITUARIES:
Bullard, W. N., 179
Forel, A., 1303
Mills, C. K., 170
Obstetrics, psychotherapy in obstetrics and gynecology, 1086
Oculogyric crises in epidemic encephalitis, 1348
Olfactory Sense: See under Smell
Oligodendroglia: See Neuroglia
Oligodendrogliomas; clinicopathologic study, *279
Olkon, D. M.: Epilepsy of angiospastic variety in monozygotic twins, 886
Ophthalmoplegia: See Eye, paralysis
Optic chiasm, chiasmal syndrome produced by chronic local arachnoiditis, 850
Ornsteen, A. M.: Clonic oculogyric crises in epidemic encephalitis, 1348
Gliomatous cyst of spinal cord in a boy 16 years of age, 678
Osteomyelitis, multiple tumors of skull simulating osteomyelitis, *393
nontraumatic osteomyelitis of flat bones of skull, 449
Overholser, W.: Psychiatric aspects of crime, 1328
Oxycephaly, 195
Oxygen, cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of a mixture of carbon dioxide and, *731

Page, H. F.: Case of parkinsonism due to manganese poisoning, 1335
Pain, cutaneous sensory fibers and sensory conduction, *1122
Palate, continuous rhythmic movements of palate, pharynx and larynx, *1236
Palsy: See Paralysis
Pancreas disease; hyperinsulinism with report of a case, 870
Papilledema: See Neuritis, optic, 1082
Paralysis, cerebral birth palsies, contribution to pathology with report of hitherto undescribed form, *524
delusional; senile, paranoia, 639
familial spastic, 227
general, encephalographic studies in, 860
general, fever treatment for dementia paralytica by means of diathermy and electric blanket, 662
general, indications for and importance of vaccine pyrotherapy in treatment of dementia paralytica, 649
general, juvenile dementia paralytica occurring in third generation of a syphilitic family, 665
ginger, histopathology of triorthocresyl phosphate poisoning: etiology of so-called ginger paralysis (third report), *976
indistinct type of Cestan-Chenais bulbar syndrome: paralysis of ninth, tenth and eleventh cranial nerves and a slight left hemiparesis, 635
Landry's, clinical and pathological study, 418
method of exciting incipient movement in weakened and paralyzed muscles, 436
ocular, anatomicoclinical observations of paralysis of movements of laterality of eyes, 405
ocular, postdiphtheric levogyric paralysis of eyes, 208
oculomotor, examination of, 1308
of lateral movements of eyes and dissociated nystagmus in multiple sclerosis, 409
of lateral movements of eyes from pontile lesion; study of oculogyric pathways, 402
spastic, sympathetic ramisection in; end-result of 60 cases, 214
Paranoia: See under Paralysis, delusional
Paraplegia, cortical, traumatic, 196
Parathyroid, investigation of anticonvulsive power of calcium alone or associated with parathyroid or irradiated ergosterol in epileptic persons, 646
Paresis: See Paralysis, general
Parinaud's Syndrome: See Eye, movement
Parkinson's Disease, Parinaud's syndrome appearing suddenly in course of, 634
phenomena of propulsion, retropulsion and lateropulsion in patients affected with, 1080
Parkinsonism due to manganese poisoning, 1335
due to poisoning by carbon disulphide, 205
incipient parkinsonism; group of objective symptoms of value in its early recognition, *392
postencephalitis, occurrence of so-called "amyloid bodies" in ganglion cells of substantia nigra in, 647
symptomatic; Parkinsonism following carbon monoxide poisoning, 1315
Paskind, H. A.: Familial spastic paralysis, 227

Patten, C. A.: Case of parkinsonism due to manganese poisoning, 1335

Pellagra with neurologic manifestations, 438

Penfield, W.: Classification of gliomas and neuroglia cell types, *745, 876

Perimetry: See Vision

Peritonitis, nerve pathways in vomiting of, 1081

Personality, abnormal personalities, 1332

measurement of depression-elation and its relation to a measure of extraversion-introversion, 426

psychoanalytic conception of depersonalization, 207

rigid personality as a factor in psychoses, *359

Petrous Bone: See under Temporal Bone

Pharynx, continuous rhythmic movements of palate, pharynx and larynx, *1236

Phosphorus, high phosphorus concentrations in infantile tetany, 437

Physostigmine, acute poisoning with, 1082

Pia Mater: See also Meninges

productive-degenerative form of endarteritis of small pial vessels: report of case showing unusual clinical and histologic features, *993

Pick's Disease: See Brain, atrophy

Pick-Niemann's Disease: See Niemann-Pick's Disease

Pigmentation, action of certain autonomic drugs upon pigmentary responses of fundulus, 866

Pike, F. H.: Monobromated camphor; a standardized convulsant, *156

Pilocarpine, action of atropine in counteracting effects of pituitrin and of pilocarpine injected into cerebral ventricles, 1314

similarity in response to posterior lobe extract (pituitrin) and to pilocarpine when injected into cerebral ventricles, 1314

Pituitary Body and narcolepsy, 425

basophilic adenoma of hypophysis with associated pluriglandular syndrome, report of case, *593

centers of hypophysis cerebri, 1321

disorders induced by injury to pituitary and hypothalamus, 658

fetal adenoma of hypophysis and dermoid cyst of hypothalamus, 202

hyperglycemia in hypopituitarism with glandular treatment, 656

squamous epithelial rests in hypophysis cerebri, *966

tumor, case of, 864

Pituitary Extract, action of atropine in counteracting effects of pituitrin and of pilocarpine injected into cerebral ventricles, 1314

reaction to posterior pituitary extract (pituitrin) when introduced into cerebral ventricles, 1313

similarity in response to posterior lobe extract (pituitrin) and to pilocarpine when injected into cerebral ventricles, 1314

use of solution of pituitary in herpes zoster, 653

Pituitrin: See Pituitary Extract

Pointing test, localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 184

Polycythemia vera, 231

Polyneuritis: See Neuritis, multiple

Posture, adequate electrical stimuli for posture and movement, 1322

Pouppirt, P. S.: Iodobismitol in treatment for neurosyphilis, *1220

Pregnancy, papillary edema during pregnancy cured by lumbar puncture, 1082

Premature infant, glioma in fourth ventricle of, *1234

Protein in spinal fluid: See Cerebrospinal Fluid, protein

Pseudosclerosis, anatomic changes in a case of Westphal-Strümpell pseudosclerosis, 856

Psychiatry, are neurology and psychiatry separate medical entities? 431

clinical psychiatric service on a part time basis; advantages and disadvantages, 436

orientations of training and practice in, 218

Psychoanalysis, an initial visit, 1104

Freud's theory of instinct and other psychobiological theories, 629

present status of psychoanalysis as a psychologic and therapeutic system, 1108

schizophrenic psychoses: critical considerations of psychoanalytic treatment, *815

Psychomotor functions, constitutional variations of, and their relationship to physique and character, 199

Psychoneuroses: See under Neuroses; Psychoses

Psychoses: See also Insanity; Mental Diseases; etc.

associated with myxoedema, 428

due to drug addiction, 216

in climacteric and involutional periods, 414

manic-depressive, blood-cerebrospinal fluid barrier in, ratios of distribution of bromide, calcium, sugar and chlorides, *829

rigid personality as a factor in psychoses, *359

spinal drainage in alcoholic deliria and other acute alcoholic psychoses, 216

Psychotherapy in obstetrics and gynecology, 1086

Pupils, quantitative measurement of pupillary and light reactions, 1100

Purkinje neurons, developmental disturbances of, 426

Putnam, T. J.: Myelotomy in treatment for syringomyelia, 889

Pyemia, changes in central nervous system in, 845

Quadrigeminate plate, tumors, 1067

Quinan, C.: Time and lineage factors of handwriting; experimental study based on specimens secured from 200 normal persons and from 148 persons with dementia paralytica, *333

Ramisection, sympathetic ramisection in spastic paralysis: end-results of 60 cases, 214

Ranson, S. W.: Contralateral flexor reflex, rebound phenomena, co-contraction and reciprocal innervation in spinal and in decerebrate cats, *247

Cutaneous sensory fibers and sensory conduction, *1122

Sensory fibers in spinal nerves, 886

Raynaud's Disease, association of Raynaud's disease with cerebral symptoms, 865

Raynaud's Disease—Continued
evidence that it is a type of vasomotor neurosis, *687
Reading, difficulty in reading (medical problem that became a psychological problem), 862
Recklinghausen's Disease: See Neurofibromatosis
Red Nucleus: See Tegmental nucleus
Reflexes, certain reflexes, especially oculocardiac reflex and provoked nystagmus, in a case of pathologic sleep, 413
clinical value of a new reflex in chorea, 863
contralateral flexor reflex, rebound phenomena, co-contraction and reciprocal innervation in spinal and in decerebrate cats, *247
galvanic skin-reflex, *146
grasping reflex in new-born monkey, *784
investigation on origin of early hypertonia and of neck reflexes of Magnus and DeKleyn, 631
localization of vestibular reaction of extended arms and of pointing test; diagnostic value of these reactions in course of diseases of cerebellar fossa, 184, 186
plantar reflexes in normal adults, *1027
quantitative measurement of pupillary and light reactions, 1100
torticollis and righting reflexes and tonic reflexes of neck, 441
vestibulocapillary reflex, 425
Respiration, neuro-anatomy in respiratory failure: report of 2 cases, *754
respiratory sequelae in a case with syndrome of posterior lacerated foramen, 15 years after traumatism, 203
Respiratory quotient: See Metabolism
Retina, cerebral circulation; changes in human retinal circulation and in pressure of cerebrospinal fluid during inhalation of mixture of carbon dioxide and oxygen, *731
variations in retinal arterial tension following nasal operations, 645
Retinoblastoma, extension of glioma (retinoblastoma) into optic nerve, 642
Rhinorrhea, cerebrospinal, 866
Rib, cervical; traumatic lesion of brachial plexus with symptoms simulating cervical ribs, 1085
Richter, C. P.: Grasping reflex in new-born monkey, *784
Injury and repair within sympathetic nervous system; preganglionic neurons, *485
Rosett, J.: Induction of sleep in epileptic persons, *131
Rothschild, D.: A productive-degenerative form of endarteritis of small pial vessels; report of case showing unusual clinical and histologic features, *993
Blood-cerebrospinal fluid barrier in manic-depressive psychosis; ratios of distribution of bromide, calcium, sugar and chlorides, *829

Sachs, B.: Presidential address, *1119
Salts, mechanism of action of blood-letting on metabolism of water and salts, 1079
Savitsky, N.: Epileptic attacks 16 years after trauma of head; operation, 1087
Schaub, C. F.: Spasmodic torticollis, *1043
Scheftel, Y.: Merzbacher-Pelizaeus disease (familial centrolobar sclerosis), 227
Schilder's Disease: See under Encephalitis
Schizophrenia: See Dementia Praecox
Schlafer, N. H.: Fracture of skull with injury of brain; diagnosis of laceration of orbital surface of frontal lobes, *583
Sciatica, surgical treatment for chronic sciatic pain, 1350
Sclerosis, disseminated sclerosis in north Wales, 1079
Merzbacher-Pelizaeus disease (familial centrolobar sclerosis), 227
Merzbacher-Pelizaeus disease, familial disease related to, 226
multiple, cause of death in, 863
multiple, intestinal worms as an etiologic factor in, 866
multiple, paralysis of lateral movements of eyes and dissociated nystagmus in multiple sclerosis, 409
Sclerosis—Continued
multiple, pathogenesis of, 641
multiple, pathology of, 1321
multiple, pathology of ganglion cells in, 862
Scotoma, hemianopic macular scotoma with hemiachromatopsia, 859
sensitive methods for detection of bjerrum and other scotomas, 645
Sea-sickness and labyrinthine theory, 213
ketosis in, 865
note on, 433
Secretions, Internal: See Endocrine Glands
Seegal, B. C.: Local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092
Seegal, D.: Local anaphylactic inflammation (Arthus phenomenon) in brain of rabbit, 1092
Sensory fibers and sensory conduction, cutaneous, *1122
Serotherapy, neuritis and multiple neuritis following, 1353
Sexual perverts and the neurotic character, 1095
Silverstein, A.: Atrophy of limbs as a sign in involvement of parietal lobe, 237
Cerebral muscular atrophy as significant sign of tumor of parietal lobe, 670
Tumor of parietal lobe, 1342
Simpson, S. L.: Raynaud's disease; evidence that it is a type of vasomotor neurosis, *687
Singer, H. D.: Disturbances of speech and praxia in organic lesions of brain, 1102
Sinuses, anatomic variations of cranial venous sinuses; their relation to effect of jugular compression in lumbar manometric tests, *801
Skin, color changes in excised and intact reptilian skin, 435
cutaneous sensory fibers and sensory conduction, *1122
galvanic skin-reflex; further aspects in psychopathologic groups, *146; correction, 400
high electrical resistance of skin of new-born infants and its significance, 437
Sleep, certain reflexes, especially oculocardiac reflex and provoked nystagmus in case of pathologic sleep, 413
induction of sleep in epileptic persons, *131
narcolepsy, *50
narcolepsy and pituitary body, 425
Smell, olfactory sense of adult meal-worm beetle, Tenebrio molitor (Linn), 207
Smith, M. I.: Histopathology of triorthocresyl phosphate poisoning; etiology of so-called ginger paralysis (third report), *976
Smith, P. E.: Disorders induced by injury to pituitary and hypothalamus, 658
Society, American Neurological Association, officers, 401
First International Neurological Congress, presidential address, *1119
First International Neurological Congress, transactions, 1301
twelfth annual meeting of Association for Research in Nervous and Mental Disease, 1300

Society Transactions:
Boston Society of Psychiatry and Neurology, 447, 889, 1328
Chicago Neurological Society, 224, 446, 662, 881, 1100
Los Angeles Society of Neurology and Psychiatry, 868
New York Academy of Medicine, Section of Neurology and Psychiatry, 217, 655, 1104
New York Neurological Society, 1087
New York Neurological Society and New York Academy of Medicine, Section of Neurology and Psychiatry, 438, 872
Philadelphia Neurological Society, 230, 451, 664, 887, 1335
Sodium amytal, effects of inhalation of carbon dioxide and oxygen and intravenous sodium amytal on certain neuropsychiatric conditions, 644
iodide in herpes zoster, 865

Somato-neuro-psychic development, new familial malady characterized by a congenital cataract and an arrest of somato-neuro-psychic development, 854
Sommer, F. C.: A new apparatus for replacement of cerebrospinal fluid by air in encephalography and ventriculography, 1337
Spasm, continuous rhythmic movements of palate, pharynx and larynx, *1236
remarks on some forms of spasms in childhood: their cause and treatment, 194
Speech, disturbances of speech and praxia in organic lesions of brain, 1102
how we reach an understanding of speech and later of reading and writing, 1085
stuttering, 643
Spekter, L.: Effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226
Spinal Cord: See also Meninges; Nervous System
bubble technic to increase efficiency of lumbar sac medication, *1058
changes in lymphogranulomatosis, *1009
gliomatous cyst of spinal cord in a boy 16 years of age, 678
hematomyelia, 1349
intramedullary neoplasm of cord with hematosyringomyelia, 873
softening; transverse myelitis with apoplectiform onset; clinical and pathologic contribution to study of myelomalacia, 202
subacute combined degeneration of cord; changes following liver therapy; histopathologic study, *1195
surgery, chordotomy of second cervical segment for relief from pain due to recurrent carcinoma of breast, 443
Spinal Puncture, demonstration of Wechselmann lumbar puncture needles, 230
Spondylitis, Kümmell's, 439
Stammering: See under Speech
Stanley, O. O.: Encephalitis with unusually light eosinophilia, *1251
Stekel, Wilhelm: critical review of work of, *1257
Stellate ganglia, effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226
Stevenson, L.: Tumors of cerebellum, 875
Stomach, hog's, in treatment of pernicious anaemia, 434
Stone, T. T.: Continuous rhythmic movements of palate, pharynx and larynx, *1236
Familial spastic paralysis, 227
Stookey, B.: Chordotomy of second cervical segment for relief from pain due to recurrent carcinoma of breast, 443
Differential section of dorsal root of trigeminal nerve, 442
Strecker, E. A.: Have psychologic concepts a practical value in neuropsychiatry, 219
Stupor, certain fundamental cerebral signs and symptoms and their response to dehydration, 455
effects of inhalation of carbon dioxide and oxygen and intravenous sodium amytal on certain neuropsychiatric conditions, 644
Stuttering: See under Speech
Substantia nigra, histopathology of, 1326
Sugar in spinal fluid: See under Cerebrospinal Fluid
Sulphur, use of sulphur for production of fever, *102
Suprarenals, effects of absinth on cat, following bilateral adrenalectomy, 651
preparation, synergistic action of atropine and epinephrine on intrinsic muscles of eye, 649
Sympathectomy, anatomic basis of, 444
Syphilis, cerebral, uncommon case of, 1325
clinical aspect of serologic discord in, 652
horizontal nystagmus with changing direction according to suppression of vision of one or other eye; tonic and kinetic disturbances of eyes following traumatism in syphilitic, 190
Syphilis—Continued
incidence in insanity, 437
iodobismitol in neurosyphilis, *1220
juvenile dementia paralytica occurring in third generation of a syphilitic family, 665
myelitis occurring in primary and in secondary stage of, *167
treatment of neurosyphilis, 436
Syringomyelia, intramedullary neoplasm of cord with hematosyringomyelia, 873
myelotomy in treatment for, 889
Syz, H. C.: Galvanic skin-reflex; further aspects in psychopathologic groups, *146
correction, 400

Tabes dorsalis, increase of non-protein nitrogen and decrease of chlorides in blood following vomiting of gastric crises, 865
lingual hemiatrophy of tabetic origin, 1074
Takata-Ara test, results of Takata-Ara test in 400 cases, 893
Tartakoff, J.: Bubble technic to increase efficiency of lumbar sac medication, *1058
Taste, course of nerve fibers transmitting sensation of taste, 432
Taylor, E. W.: William Norton Bullard, 179
Taylor, W. J.: Surgical treatment for chronic sciatic pain, 1350
Teel, H. M.: Basophilic adenoma of hypophysis with associated pluriglandular syndrome, report of case, *593
Tegmental nucleus; Claude's inferior syndrome of red nucleus associated with Parinaud's syndrome, 1319
Temporal Bone, tumor of petrous bone of malpighian origin, involving dura and cranial nerves, 423
Tetany, high phosphorus concentrations in infantile tetany, 437
Thallium acetate, reaction of microglia and nerve elements to experimental poisoning by, 641
microglia and oligodendroglia in experimental intoxication by, 648
Thrombophlebitis of cavernous and intercavernous sinuses: bilateral orbital thrombophlebitis consecutive to peritonsillar abscess, 216
Thrombosis and embolism, prolonged direct observation of phenomena in pial vessels of living cat, 859
lateral sinus thrombosis complicating masked mastoiditis, 653
Thyroid, iodine deficiency and goiter: influence of a diet poor in iodine on thyroid gland in white rats, 852
extract, unilateral exophthalmos following use of, 866
Thyroidectomy, thyrotoxicosis following subtotal thyroidectomy for exophthalmic goiter, 214
Thyrotoxicosis following subtotal thyroidectomy for exophthalmic goiter, 214
Tic, facial, in hepatolenticular degeneration with severe secondary anemia resembling pernicious anemia, 419
mechanism of some convulsive movements of orbicularis and of face, 866
Timme, W.: Pluriglandular compensatory syndrome, 656
Tongue, lingual hemiatrophy of tabetic origin, 1074
Tonsillectomy, peripheral neuritis complicated by massive collapse of lung following, 212
Torticollis and righting reflexes and tonic reflexes of neck (Magnus), 441
spasmodic, *1043
Touch, experiments on use of sense of touch in relation to language, 1101
Tower, S. S.: Injury and repair within sympathetic nervous system; preganglionic neurons, *485
Toxemia, reaction types in intoxication, 420
Transplantation, growth of eyes and limbs transplanted heteroplastically between 2 species of amblystoma, 861

Transplantation—Continued
heteroplastic experiments on limb and shoulder girdle of amblystoma, 1084
Travis, L. E.: Mass responsiveness in central nervous system, *141
Trichloroethylene in treatment of trigeminal neuralgia, 433
Triorthocresyl phosphate poisoning: etiology of so-called ginger paralysis (third report), *976
Trumper, M.: Antagonistic biochemical mechanisms in diabetes and epilepsy, 1336
Tuber Cinereum: See Hypothalamus
Tumor: See also Cancer
craniopharyngeal pouch tumors, 420
ganglioneuromas of central nervous system, *501
multiple tumors of skull simulating osteomyelitis, *393
parietal lobe, 1342
petrous bone, of malpighian origin, involving dura and cranial nerves, 423
of posterior corpus callosum, 441
of posterior cranial fossa causing visual hallucinations, 2 cases, 652
Tuthill, C. R.: Elastic layer in cerebral vessels; studies of new-born and of children, *268
Twins, epilepsy of angiospastic variety in monozygotic twins, 886
identical, palm and sole patterns in, 1352
Tympanic membrane: See Ear
Tyrosine, aromatemia and aromaturia from tyrosine in dementia praecox, 633

Urine, calcium in blood and urine of patients with dementia praecox, 1317
changes in alkali reserve of blood plasma, of urinary hydrogen ion concentration, and of frequency of convulsive seizures following administration of anticonvulsive drugs and calcium chloride in epileptic persons, 1314

Vaccination, Encephalitis following: See under Encephalitis
Varicella: See Chickenpox
Vasomotor neuroses; Raynaud's disease; evidence that it is a type of vasomotor neurosis, *687
response of minute vessels of human brain to histamine, *737
Vein, internal jugular venous pressure and its relationship to pressure of cerebrospinal fluid, 892
jugular; anatomic variations of cranial venous sinuses; their relation to effect of jugular compression in lumbar manometric tests, *801
Ventriculography: See under Brain
Vertigo, laryngeal vertigo and its relation to cataplexy, 446
Vibber, F. L.: Bubble technic to increase efficiency of lumbar sac medication, *1058
Vision, binocular vision and projection, 1306
hallucinations in a visual semifield from spasm of sylvian artery, 636
moving pictures of visual fields, 242
perimetric examinations, 240
tumor of posterior cranial fossa causing visual hallucinations, 2 cases, 652
Visit, an initial visit, 1104
Vomiting, certain fundamental cerebral signs and symptoms and their response to dehydration, 454
in peritonitis, nerve pathways of, 1081
increase of nonprotein nitrogen and decrease of chlorides in blood following vomiting of gastric crises, 865
Voris, H. C.: Spasmodic torticollis, *1043

Water, mechanism of action of blood-letting on metabolism of water and salts, 1079
Wechselmann lumbar puncture needles, 230
Weights, phenomenon of false estimation of weights in mentally defective, 648
Weil, A.: Spinal cord changes in lymphogranulomatosis, *1009
Weisenburg, T. H.: Charles Karsner Mills, 170
Weiss, S.: Cerebral circulation; cerebral blood flow and vasomotor response of minute vessels of human brain to histamine, *737
Wentworth, H.: Perimetric examinations, 240
Wertham, F.: Cerebral lesions in purulent meningitis, *549
Westphal-Strümpell pseudosclerosis, anatomic changes in case of, 856
Wilgus, S. D.: Fever treatment for dementia paralytica by means of diathermy and electric blanket, 662
Wilson, G.: Hematomyelia, 1349
Neuritis and multiple neuritis following serum therapy, 1353
Wilson, J. G.: Laryngeal vertigo and its relation to cataplexy, 446
Wilson-pseudosclerosis symptom-complex, symmetrical confluent lesions in frontal lobes in, 1084
Windle, W. F.: Neurons of sensory type in ventral roots of man and of other mammals, *791
Winkelman, N. W.: Convulsive state with unusual pathologic conditions, 451
Woodworth Psychoneurotic Inventory, study of, with suggested revision, 434
Wormwood oil, effect of removal of stellate ganglia on wormwood oil convulsions in cats, *1226
Wortis, S. B.: Monobromated camphor; a standardized convulsant, *156
Wry Neck: See Torticollis

Yakovlev, P. I.: Congenital ectodermoses (neurocutaneous syndromes) in epileptic patients, *1145
Yannet, H.: Nonsuppurative encephalomyelitis accompanying chickenpox, *322
Yaskin, J. C.: Nonsuppurative, nonepidemic encephalitis following labor and in puerperium; report of case probably due to cerebral anoxemia, with a review of literature, *371
Primary fibroblastoma of brain, 1335

Zilboorg, G.: Neurotic character and the pervert, 1095
Zimmerman, H. M.: Nonsuppurative encephalomyelitis accompanying chickenpox, *322
Ziskind, E.: Hyperinsulinism, with report of a case, 870